

Mutagenic Effects of Manganese Sulfate 11/74

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MUTAGENIC EFFECTS OF
MANGANESE SULFATE

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Compound Report No. 3

STUDY OF MUTAGENIC EFFECTS OF
MANGANESE SULFATE (FDA No. 71-71)

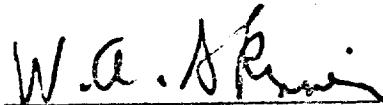
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INTRODUCTION

Under contract to the Food and Drug Administration, SRI is examining the mutagenicity of selected chemical compounds (Contract No. FDA 73-215). This report describes the results of tests conducted on manganese sulfate (FDA No. 71-71). It presents detailed descriptions of the methodologies used to perform these tests.

Four methods were used for evaluating the genetic hazards of the test compounds. These were: (1) host-mediated assay, (2) in vitro microbial assay, (3) dominant lethal test, and (4) mouse translocation test. Each procedure is described in detail below.

For the compound under consideration in this report, single and repeated oral administrations were performed at three concentrations for both the host-mediated assay and dominant lethal test. The amounts were: (1) a maximum level--the calculated LD₅ or 5 g/kg (whichever was lower); (2) an intermediate level--1/10 of the LD₅ or 1 g/kg (whichever was lower); and, (3) a low level--1/100 of the LD₅ or 200 mg/kg (whichever was lower). For manganese sulfate the maximum level was 1200 mg/kg (the LD₅), the intermediate level 120 mg/kg, and the low level 12 mg/kg.

In the mouse translocation test, the test material was fed in the diet at two dosage levels. These were: a high level--the calculated LD₅ or 5 g/kg, whichever was lower, and a low level--1/10 of the LD₅ or, in the case where 5 g/kg was used, 1 g/kg. For manganese sulfate the high level was 1200 ppm (the LD₅), and the low level was 120 ppm.

SUMMARY

Host-Mediated Assay - Mouse

Manganese sulfate (FDA 71-71) was not mutagenic in the host-mediated assay using Salmonella typhimurium TA1530, nor did it increase the mitotic recombination frequency in the host-mediated assay Saccharomyces cerevisiae D3.

In vitro Assay

In the in vitro assays, manganese sulfate was not mutagenic to S. typhimurium strains TA1535, TA1536, TA1537, and TA1538, either in the presence or absence of metabolic activation. At a concentration of 5%, manganese sulfate did not increase the mitotic recombination frequency of S. cerevisiae D3.

Dominant Lethal Test - Rat

This experimental procedure produced no consistent responses to suggest that manganese sulfate (FDA No. 71-71) is mutagenic to the rat. The positive reference compound, TEM, a known mutagen, generally produced mutagenic responses from the first through the fifth weeks of the experiment, as expected. Mathematical treatment of the dominant lethal data, conducted according to a statistical program outlined by FDA, failed to show consistent significant differences (that could be attributed to an effect of manganese sulfate) at $P < 0.01$ or $P < 0.05$.

Translocation Test - Mouse

An extensive translocation study of manganese sulfate ($MnSO_4$, FDA No. 71-71) was conducted in mice to investigate whether heritable mutagenic events occur when the compound is repeatedly ingested over an extended period.

Manganese sulfate was administered in the diet for seven weeks at two concentrations (120 and 1200 ppm), forty adult male mice per group. A similar number of control mice received the diet only during this.

time, while a positive control group received triethylenemelamine (TEM) for four weeks in the drinking water. Each male was bred to two virgin females to produce an F₁ generation, the males of which were raised to maturity. One hundred F₁ males per treatment level were bred to three virgin females. Evaluation of the pregnant females provided data that identified the nonbreeders, presumptive steriles, and partially steriles in each treatment group. Rebreeding these suspect animals reduced the number to three control, 20 TEM, and one MnSO₄ (120 ppm)-treated males. Three controls and three TEM F₁ males were subjected to cytogenetic testes evaluation of meiotic cell preparations. None of the control meiotic chromosomes showed heritable cytogenetic abnormalities, while all three TEM males each had single reciprocal translocations. The single nonbreeder MnSO₄ (120 ppm) F₁ male was not evaluated cytogenetically.

Under the conditions of this study, it is concluded that manganese sulfate (MnSO₄, FDA No. 71-71) administered in the diet over a seven-week period does not induce translocation heterozygosity in male mice.

HOST-MEDIATED ASSAY - MOUSE

Background

The host-mediated assay combines the advantages of the mammalian metabolic system with those of microbial systems for detecting mutagens or metabolites of chemicals that are not mutagenic. Microbial assays allow both the exposure of large cell populations to the chemical being tested and the determination of mutation frequencies. In addition, microbial assays are relatively inexpensive compared with other systems of detecting carcinogens. The mammalian organisms provide the metabolic activities present in mammals that are absent in microorganisms. For example, dimethylnitrosamine is not mutagenic on direct exposure to bacteria but is mutagenic in the host-mediated assay.

In the host-mediated assay, the indicator microorganism is injected into the host's peritoneal cavity at the same time the host receives the test compound by some other route, such as oral intubation or intramuscular injection. The microorganism is allowed to incubate while the animal metabolizes the compound. After the organism has had a chance to incubate, it is removed from the animal and assayed for mutations. Theoretically, during the incubation period, the organism is then exposed to whatever metabolite normally might reach the various tissues in the animal. By comparing the mutagenicity of the compound in vitro with that obtained in the host-mediated assay, it is possible to determine if any activation or deactivation of the test compound has occurred during metabolism in the animal. For this report, a detailed description of the methodology has been provided even though it has been generally outlined in the literature (e.g., E. Zeiger and D. Brusick. The host-mediated assay--a protocol for Salmonella and Saccharomyces. Newsletter of the Environmental Mutagen Society 5, 32-34, 1971).

Materials and Methods

Microorganisms

A histidine auxotroph of Salmonella typhimurium TA1530 was used in these studies to measure biochemical reversion mutations. The yeast Saccharomyces cerevisiae D3 which is a diploid organism heterozygous for two linked genes (ade2 and his8), was used to measure for mitotic recombination.

Animals

Male Swiss albino mice, weighing an average of 28-30 g, were used for this study and maintained on a diet of Purina Lab Chow. The mice were obtained from Simonsen Laboratories, Gilroy, California.

Preparation of Microorganisms for Inoculation

The Salmonella strains were maintained on tryptone-yeast extract agar slants. To prepare the organism for inoculation into mice, a small inoculum from an agar slant was added to a broth consisting of 1.0% tryptone and 0.5% yeast extract. This culture was incubated for 24 hr at 37°C. The resulting suspension of cells was then adjusted to a concentration of $3-5 \times 10^8$ viable cells/ml using a spectrophotometer.

The yeast strain was maintained on yeast extract (0.5%) glucose (5.0%) agar slants. To prepare the yeast for inoculation into mice, a small inoculum from the agar slant was added to a broth consisting of 5% glucose, 0.5% yeast extract, and 0.2% peptone. This culture was incubated on a rotary shaker at 30°C for 24 hr. The cell concentration was adjusted spectrophotometrically to a concentration of $1-3 \times 10^8$ viable cells/ml before inoculating the animals.

Inoculation of the Mice

Two ml of the appropriate organism was inoculated into the peritoneal cavities of the mice using a 23-gauge needle. The area of inoculation was washed with ethanol before injection. The test compound was administered simultaneously with the inoculation.

Administration of Test Compound

The test compounds were administered by oral intubation using an 18-gauge intubating needle. The compound was dissolved in water or suspended in Mazola pure corn oil to a concentration requiring a 0.4 ml volume for each intubation.

The positive control compound for Salmonella, dimethylnitrosamine (DMNA), was dissolved in 10% ethanol to a concentration that would provide a 30-g mouse with a dose of 100 mg/kg. The positive control for the yeast, ethyl methane sulfonate (EMS), was dissolved in sterile saline to give a dose of 350 mg/kg/mouse. Positive control compounds were administered in 0.10 ml volumes by intramuscular injection.

Negative controls were run in all experiments. The negative control consisted of administering the solvent used for the test compound by oral intubation.

Autopsy and Recovery of Organisms

All test groups were sacrificed 4 hr after inoculation of the organism and administration of the test compound. The mice were sacrificed by cervical dislocation, their exterior abdominal regions were washed with ethanol, and 2 ml of sterile saline were injected into the peritoneal cavity of each mouse. The peritoneal cavity was opened aseptically, and the exudate withdrawn using a tuberculin syringe without a needle. The peritoneal exudates from each mouse were treated individually. They were placed in sterile tubes and immediately put in an ice bath. All plating of the samples was begun immediately after removal from the mouse.

Enumeration of Total Viable and Mutant Cells

Tenfold serial dilutions were made for each peritoneal exudate by serially adding 0.5 ml of sample to 4.5 ml of sterile saline. For the bacteria, a concentration series from 10^0 to 10^{-7} was prepared and for the yeast a series from 10^0 to 10^{-5} .

To enumerate total viable bacteria, the 10^{-6} and 10^{-7} dilutions were plated by adding 0.1 ml of sample/plate to 3 separate plates.

Each sample was spread over the surface of the plate using a sterile, bent glass rod. The medium used to enumerate total viable cells was as follows:

<u>Bacteria Complete Medium</u>	
Trypt	
Yeast	0.5%
Agar	2.0%
Dist. H ₂ O	to desired volume

To enumerate the revertant mutant bacterial cells, the 10^0 (and the 10^{-1} dilution if a large number of revertants were expected) dilutions were plated as described for enumerating the total bacteria. Six plates were used for each sample. The medium used for enumerating mutants was as follows:

Bacteria Minimal Medium

(NH ₄) ₂ SO ₄	0.2%
K ₂ HPO ₄	1.4%
KH ₂ PO ₄	0.6%
Na citrate	0.1%
MgSO ₄	0.02%
Biotin	0.5 µg/ml
Glucose	0.5%
Agar	
Dist. H ₂ O	to desired volume

The glucose and biotin were sterilized separately and added to the autoclaved salt solution.

All bacteria were incubated at 37°C, the bacteria complete plates for 18 hr, and the bacteria minimal for 40 hr. If the plates could not be counted at this time, they were refrigerated.

To enumerate the yeast (both total viable cells and mitotic recombinants), samples from the 10^{-2} to 10^0 dilutions were plated on a yeast complete medium. They were plated in the same manner described for the enumeration of the total bacteria. Total viable counts were

usually obtained by counting the 10^{-5} or 10^{-4} plates. The number of mitotic recombinant colonies was usually obtained by scanning the 10^{-3} or 10^{-2} plates with a dissecting scope at 10 X. The mitotic recombinants were seen as either red colonies or as red sectors on a normally white yeast colony. The prominence of the mitotic recombinants was enhanced by refrigerating for several days following the normal incubation of the yeast at 30°C for 48 hr.

The medium used for plating yeast was as follows:

Yeast Complete Medium

Yeast extract	0.5%
Peptone	0.35%
Glucose	2.0%
Agar	2.5%
KH_2PO_4	0.15%
$\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$	0.05%
$(\text{NH}_4)_2\text{SO}_4$	0.45%
Dist. H_2O	to desired volume

Data Handling

The data from all mice were used unless a great deal of contamination occurred or low recovery rates were obtained, possibly because the organism might have been injected into some organ rather than the peritoneal cavity. The number of colony forming units (CFU) or mitotic recombinants was determined by:

$$\frac{\text{No. CFU/plate}}{\text{No. plates}} \times \frac{1}{0.2} \times \frac{1}{\text{dilution factor}} = \text{CFU/ml in undiluted exudate}$$

The mutation frequency (MF) was calculated by:

$$\text{MF} = \frac{\text{total mutant cells}}{\text{total population}}$$

Treatment Groups

All treatment groups, including the positive and negative controls, consisted of 10 mice. The method used to determine concentrations of test compound is described in the section on the dominant lethal test.

The following groups were tested for all three organisms:

Group	Treatment	Day of Treatment on which Test Organism was Injected
1	Maximum tolerated dose	1
2	Intermediate dose	1
3	Low dose	1
4	Appropriate positive control	1
5	Appropriate negative control	1
6	Maximum tolerated dose	5
7	Intermediate dose	5
8	Low dose	5
9	Appropriate negative control	5

For testing FDA no. 71-71, the following doses were used:

Maximum dose - 1200 mg/kg
Intermediate dose - 120 mg/kg
Low dose - 12 mg/kg

In vitro Tests

The method described by Ames was used to determine in vitro mutagenicity for the bacteria (B. N. Ames, W. E. Durston, E. Yamasaki, and F. D. Lee. Proc. Nat. Acad. Sci. U.S.A. 70, 2281-2285, 1973).

To determine the in vitro mitotic recombination frequency of the test compound on the yeast, it was first necessary to determine what level of the test compound gave a 50% survival of the organism after a 4-hr exposure at 30°C. If the compound showed no lethal effects, a concentration of 5.0% w/v was used. In the actual test for mitotic recombination, the yeast (approximately 5×10^7 cells/ml) was exposed to the appropriate concentration of compound for 4 hr, and then samples were plated as described for determining mitotic recombinants in the section on host-mediated assay. The mitotic recombination frequency is expressed as sectors per 10^5 survivors. This was compared with a negative control.

In the yeast in vitro studies, EMS was employed as the positive control. In the bacterial in vitro assays, 2-fluorenamine was employed as the positive control for metabolic activation.

Results and Discussion

Host-Mediated Assay

Table 1 summarizes the results of the host-mediated assay of manganese sulfate (FDA No. 71-71) with Salmonella typhimurium TA1530. (The data for individual mice are presented in Tables 3 and 4.) We conclude that manganese sulfate is not mutagenic to S. typhimurium strain TA1530 at the doses tested when given as a single or multiple oral treatment in the host-mediated assay. The known mutagen DMNA significantly increased the reverse mutation frequency of TA1530.

In the calculation of the average number of histidine-positive revertants per 10^8 CFU, we have included values that vary greatly among different mice in the same experiment (e.g., Table 4--mouse 1, 12 mg/kg dose of manganese sulfate, and mouse 2, 1200 mg/kg dose of manganese sulfate). These "outliers" may skew the results. In general, the outliers are associated with poor recovery of the microorganism from the peritoneal cavity.

Table 2 summarizes the results of the host-mediated assay with Saccharomyces cerevisiae D3. (The data for individual mice are presented in Tables 5 and 6.) Manganese sulfate did not increase the mitotic recombination frequency of S. cerevisiae D3 at the doses tested when given as a single or multiple oral treatment. The known mutagen EMS significantly increased the mitotic recombination frequency of S. cerevisiae D3.

In vitro Microbial Assay

In the in vitro assays, manganese sulfate was not mutagenic to S. typhimurium either in the presence or absence of the metabolic activation system (Table 7). At a concentration of 5%, manganese sulfate was not toxic to nor did it increase the mitotic recombination frequency of S. cerevisiae D3 (Table 8).

We therefore conclude that manganese sulfate, FDA No. 71-71, is not mutagenic toward the S. typhimurium strains we have tested, nor does it increase the mitotic recombination frequency of S. cerevisiae D3.

DOMINANT LETHAL TEST - RAT

Background

Dominant lethal assays of compounds suspected of causing major genetic damage in animals have been carried out, for the most part, in mice. One exception was a comparative study by Bateman with mice and rats to evaluate the dominant lethal effect of triethylenemelamine (*Genet. Res. Camb.* 1, 381-392, 1960). Although there are cost savings in using the mouse rather than the rat, the latter has experimental advantages in providing more definitive information when attempting to assess the incidence of early fetal deaths. Also, corpora lutea counts in the mouse are difficult and relatively imprecise (S. S. Epstein and G. Rohrborn, *Nature* 230, 469-470, 1971). For this project, adult Sprague-Dawley-derived rats, from a closed random-bred colony, were used for the acute toxicity determinations as well as the dominant lethal assay.

In the mammalian test procedure, the compound under investigation was administered orally either once or on five successive days to proven male breeders. Following dosing, each male was mated with two adult female rats for seven days. The females were then removed, and new females again were added for another week of breeding. This sequence continued for eight weeks. Thus, the procedure is designed to indicate possible mutagenic effects on the male sperm, with the normal female acting as a carrier to demonstrate abnormalities that may have occurred in the male. Effects were evaluated by examining the state of fetal development during the middle to latter stages of gestation.

The experimental approach is presented below in a step-by-step manner to ensure clarity and an understanding of the preciseness of procedures used in this phase of the program.

Materials and Methods

Animals

Adult male and female Sprague-Dawley-derived rats were supplied by Simonsen Laboratories, Gilroy, California. The males were proven breeders, while the females were of virgin stock. Purina Lab Chow and water were available at all times.

Chemical Supply

All compounds or natural materials were supplied by the Food and Drug Administration. Each compound or natural material was provided in a ready-to-use form and was identified by both name and FDA code number. Sufficient quantities to complete all aspects of the experimental program were received. Excess supplies were placed in storage, should they be needed for future reference.

Solubility Studies

Solubility of each compound or natural material was investigated using such agents as water, propylene glycol, polyethylene glycol, corn oil, tricaprylin, carboxymethylcellulose, or methylcellulose (Methocel) to determine the most appropriate vehicle for administration. Because of the low toxicity of most materials and the consequent high dosages required, many of the test materials were administered as suspensions.

Acute Toxicity (Single and Multiple Dose)

Although acute toxicity information on some of the compounds was available in the literature, confirmatory tests were done to obtain an LD₅₀ under our laboratory conditions and for this strain of rat. If no data were available, a broad, range-finding dose regimen was conducted, followed by an accurate determination of the oral LD₅₀.

A range-finding dose regimen was conducted using the acute data to determine an accurate multiple dose LD₅₀. Nonstarved animals were used throughout this part of the study because of the multiple dosing regimen.

Dosage Selection

In selecting the three dosage levels for the experimental study, two approaches were used:

- (1) If a finite LD₅₀ was obtained, the highest dose level was the calculated LD₅. The intermediate dose was 1/10 of the calculated LD₅, and the lowest dose was 1/100 of the calculated LD₅.
- (2) If the LD₅₀ was greater than 10 g/kg (a mutually agreed on upper limit), the highest dose was 5 g/kg; the lowest dose was 200 mg/kg; and the intermediate dose was 1 g/kg. These guidelines were used for both single and multiple dose experimental study groups.

Control Groups (Vehicle and Positive)

A vehicle control group (corn oil, water, Methocel, etc.) was included in each experimental study. Vehicle control animals were included in both the acute and subacute studies. In this manner, breeding and implant data were obtained for each vehicle control and were used as reference comparisons for the experimentally treated animals, both the single and multiple treatment groups. The positive reference control was the known mutagen, triethylenemelamine (TEM), given at a dose of 0.2 mg/kg as a single i.p. injection. Breeding and implant data were obtained for eight weeks.

Acute Studies (Single Dose)

In an acute study, ten experienced breeder male rats per treatment group were administered a single oral dose of test compound. Controls were treated as previously described. Within two or three hours of dosing, each male was presented with two virgins of breeding age for a period of seven days. Females were replaced weekly over a total mating period of eight weeks.

Subacute Studies (Multiple Dose)

For the subacute assay, the experimental parameters used in the acute test were employed, with three exceptions: (1) five dosings

were given at 24-hour intervals; (2) weekly mating periods lasted for seven rather than eight weeks; and (3) the same positive control group used for the acute dosing also served as the reference group for the subacute assay.

Necropsy

Starting two weeks after the first day of breeding, one-fourth of the pregnant females in each group were sacrificed on four successive days. This schedule allowed for sacrifice of females between 11 and 18 days of pregnancy. A complete autopsy of each female was done to determine if there was intercurrent infection, since such a condition can induce preimplantation loss and early fetal deaths (G. Rhorborn, *Humangenetik* 6, 345, 1968).

Observations

At time of sacrifice, each female was scored for early fetal deaths, late fetal deaths, living fetuses (all of which provide a total implant score), corpora lutea, and pre-implantation loss (determined by subtracting the total implant score from the total corpora lutea score).

Evaluation

The following parameters indicate effects in dominant lethal studies: total implants (live fetuses plus early and late fetal deaths), total dead (early and late fetal deaths), dead implants per total implants, and pre-implantation loss (calculated as the difference between the total corpora lutea and total implant counts). We also evaluated total corpora lutea because a significant change of this parameter could influence the significance of the pre-implantation loss. Total implants, total dead, total corpora lutea, and pre-implantation loss parameters were analyzed for significance by the t-test.

The index of dead implants per total implants was analyzed statistically by the t-test on arcsine (or angular) transformed data, as described in Experimental Design (Theory and Application),

by Walter T. Federer, The Macmillan Company, 1955. This index was computed for each female.

The assumptions underlying the analysis of variance and the usual tests of significance are discussed by C. Eisenhart (*Biometrics* 3, 1-21, 1947); W. G. Cochran (*Biometrics* 3, 22-38, 1947) discusses the consequences when the assumptions underlying the analysis of variance are not fulfilled. These two papers, plus one by Bartlett (*The use of transformations. Biometrics* 3, 39-52 and 96, 1947), provide background information on this subject.

Results and Discussion

Single and multiple dose toxicity data are presented below.

Oral Toxicity - Rat and Mouse

Compound: Manganese Sulfate
FDA No.: 71-71

	<u>Rat</u>	<u>Mouse</u>
Single dose ^a	2.39 g/kg	2.33 g/kg
Multiple dose ^b	> 1.8 g/kg	> 1.5 g/kg

^aTen male, Sprague-Dawley rats, weighing 285-368 grams each, and ten male, Swiss Webster mice, weighing 18-22 grams each, were fasted overnight and then administered orally specified amounts of the candidate compound dissolved or suspended in water.

^bTen male, nonfasted Sprague-Dawley rats, weighing 264-310 grams each, and five male, nonfasted Swiss Webster mice, weighing 17-24 grams each, were administered orally specified amounts of the candidate compound dissolved or suspended in water.

After an evaluation of the toxicity data, dosage levels for the mutagenesis assays were selected as follows:

Single dose--1200 mg/kg, 120 mg/kg, and 12 mg/kg

Multiple dose--1200 mg/kg, 120 mg/kg, and 12 mg/kg.

Throughout the experiment, the biological criteria used to evaluate mutagenic effects in the rat showed no consistent responses that could be attributed to treatment. There were occasional statistical differences between control and manganese sulfate dosed groups, but they were random and did not suggest a time or dose-response effect.

Table 9 presents summary data on the implantations per pregnant female, Table 10 summarizes dead implants per pregnant female, Table 11 summarizes dead implants per total implants, Table 12 summarizes corpora lutea per pregnant female, and Table 13 summarizes pre-implantation loss per pregnant female.

Appendix A presents a description of the statistical analysis procedures used for dominant lethal tests with an explanation of the computer printouts.

Appendix B contains computer printouts of the raw data and the statistical analyses.

Careful review and statistical evaluation of the data do not show manganese sulfate ($MnSO_4$, FDA No. 71-71) to be a mutagen in the rat by the dominant lethal test.

HERITABLE TRANSLOCATION TEST - MOUSE

Background

Human populations frequently are exposed to man-made chemicals for extended periods, and often at borderline detectable levels. To evaluate the genetic hazards of such chemicals, it is considered prudent that such materials be studied in mammalian systems at several dosages in order to maximize detection of a mutagenic response.

Chemical induction of chromosomal aberrations in the mouse is an important experimental tool, in view of the many human genetic defects that are due to various chromosomal anomalies. To date, evaluations of chemically induced chromosomal aberrations have been attempted with the dominant-lethal test and cytogenetic studies of somatic and germinal cells of certain mammals. Although these test procedures can provide useful information, they do not measure heritable genetic effects. Obviously, the most important mutagenic effects are permanent and transmissible. A need has existed, therefore, for a method which can reliably identify compounds that cause heritable chromosomal aberrations in mammalian systems. The mouse translocation procedure would appear to be such a system.

A well-defined translocation test will determine the fertility of an F_1 male population derived from F_0 males treated with a test agent. Confirmation of a sterile or a partially sterile response can be obtained by cytological examination of the germ cells from suspected males. Sterility and partial sterility are closely correlated with the induction of translocation heterozygotes.

The procedure used in conducting this translocation test was based on experimental techniques described by Leonard and DeKnudt (Mutation Research 9, 127, 1970), Cattanach et al (Mutation Research 6, 297, 1968), Falconer et al (J. Genetics 51, 81, 1952), and Generoso (Meeting Environmental Mutagen Society, March 1971, p. 9, Abstracts); modifications of approach were made by staff of this laboratory in consultation with staff of the Genetic Toxicology Branch, Bureau of Foods, FDA.

Materials and Methods

Animals

Adult male and female ICR/SIM mice were supplied by Simonsen Laboratories, Gilroy, California. The F₀ males, used in the test compound treatment groups, were three- to four-month-old proven breeders. Females, used in the breeding phases, were 9- to 10-week old virgins.

Chemical Supply

All materials for evaluation were supplied by the Food and Drug Administration with the exception of N-methyl-N'-nitro-N-nitrosoguanadine (MNNG), which was purchased by SRI from Aldrich Chemical Co., San Leandro, California. Sufficient quantities to complete all aspects of the experimental program were received. Excess supplies have been placed in storage, should they be needed for future reference.

Acute Toxicity (LD₅₀)

Although acute toxicity information on some of the compounds was available in the literature, confirmatory tests were conducted to obtain an LD₅₀ under our laboratory conditions and for this strain of mouse. If no data were available, a broad, range-finding dose regimen was conducted, followed by an accurate determination of the oral LD₅₀.

Dosage Selection

Two treatment levels were used in the translocation test. In selecting these levels, two approaches were used:

- (1) If a finite LD₅₀ response was obtained, the maximum dose was the calculated LD₅; the lower dose was 1/10 of the calculated LD₅.
- (2) If the LD₅₀ was greater than 10 g/kg (a mutually agreed-upon upper limit), the maximum dose was 5 g/kg; the lower dose was 1 g/kg.

Reference Control

Two reference control groups were included in this contract program. One was run at the beginning of the series of translocation tests; the other was done at the end of the test series. In this manner, breeding and implant data were obtained at two separate time periods, as well as providing an increased reference-control data base. F_0 males in these groups were fed a finely ground commercial laboratory diet with corn oil added at a level of 2%; thereafter, all animals in these groups were fed a commercial pelleted diet. Water was available ad libitum. Control groups were treated in the same manner as compound test groups.

Positive Control

A positive control was run concurrently with a negative control.

For this group, the known mutagen triethylenemelamine (TEM) was administered initially in the drinking water (0.32 mg/l) for four weeks, at an approximate ingestion dose of 0.062 mg/kg/day. Fresh TEM solutions were prepared daily. A commercial pelleted diet was available at all times.

In this exploratory study, forty treated males bred to 81 females produced only 11 litters. The large number of sterile males and the small size of the litters showed that the dosage level was too high to allow production of sufficient numbers of offspring for adequate evaluation. A confirmatory TEM study using the same dosage regimen had been underway for two weeks when the first TEM data became available. TEM concentration was immediately reduced for the final two weeks to 0.124 mg/l, an intake level of approximately 0.024 mg/kg/day. Discussion of the results for both TEM experiments is presented in Results and Discussion.

Administration of Test Compounds

The candidate compound was fed in the diet to adult male mice for seven weeks. An appropriate amount of compound initially was dissolved or suspended in corn oil; then the compound-oil concentrate

was added at a level of 2% to a finely ground commercial diet of known composition. The use of corn oil assured even distribution of the compound and presented stratification of the test material in an otherwise dry diet. Diets prepared at two-week intervals were refrigerated at 4°C until fed to the animals. In addition, the diet was replaced in the feed containers every other day to minimize the possibility of compound loss.

Genetic Tests

After seven weeks of dietary compound treatment or four weeks of TEM drinking-water treatment, approximately 40 treated males per group were mated, each with two adult virgin females; after two weeks, each female was housed individually and allowed to litter. Impregnation time was based upon the date of parturition. Litters from the second week of breeding were discarded. Weanling females were discarded while males were raised to maturity (10-12 weeks). At maturity, 100 F₁ males per group were randomly selected and housed individually. Three adult virgin females were bred to each F₁ male for a period of two weeks; examinations were made daily for the presence of vaginal plugs. Females were sacrificed 14 days after mating; a uterine analysis was performed to determine the number of total, live, and dead implants.

Criteria for Classification of a Male as Sterile or Partially Sterile

An in-depth statistical review of breeding data from control animals was performed by Theodore W. Horner, Statistical Consultant, Division of Mathematics, Bureau of Foods, Food and Drug Administration. This review of a normal litter size distribution and discussions between the FDA and SRI technical staffs provided the necessary information for establishing the classification criteria for a male as sterile or partially sterile.

Classification of a F₁ male mouse as sterile or partially sterile was made according to the following criteria:

- "Partially Sterile" Male

- (1) If all three females are pregnant, each female must have 9 or fewer live implants---with at least one female having 6 or fewer live implants.
- (2) If two of three females are pregnant, both females must have 9 or fewer live implants---with one female having 6 or fewer live implants.
- (3) If only one of three females is pregnant, this female must have 6 or fewer live implants.

- "Sterile" Male

- (1) None of three females pregnant---previously identified by presence of a vaginal plug.

Any F_1 male that did not fit one of the above-mentioned selection criteria was considered "normal".

F_1 males found to be sterile or partially sterile were held for future evaluation (i.e., additional breeding and/or cytogenetic study of meiotic chromosomes).

Evaluation

A careful review of the F_0 breeding and litter data was conducted to determine if there were possible correlations between compound treatment and breeding performance, litter size, or sex distribution.

F_1 males were identified as sterile or partially sterile by the evaluation method outlined above. Individual data were totaled to give the number of observed F_1 males (presumptive translocations) per treatment based on the breeding of 300 females per group. Various parameters were evaluated such as percent pregnancies, average litter size, average number of males per treatment bred to females with 0 - 5 or more dead implants, average number of females per treatment with 0 - 5 or more dead implants, percent per treatment with plugs, and percent pregnancies per treatment with and without plugs.

Meiotic Cell Cytogenetic Studies

Male mice that showed characteristics of presumptive translocation after two breedings were reviewed by FDA and SRI staff members. Selected males were then evaluated for chromosomal translocations by examination of meiotic preparations of the testes. Cytogenetic studies were conducted by Dr. K. S. Lavappa, Department of Cell Culture, American Type Culture Collection (ATCC), Rockville, Maryland.

The two testes from each animal were weighed and examined separately. Meiotic preparations were made with the air-drying technique. Spermatocytes in diakinesis-metaphase I were examined for the presence of translocations. From each testis, four slides were examined and 40 spermatocytes were scored per testis.

Results and Discussion

Acute Toxicity (LD₅₀)

The LD₅₀ in mice was 2.33 g/kg with 95% confidence limits of 1.84 to 2.96 g/kg. The calculated LD₅ for this compound was 1200 mg/kg. Based on the LD₅₀ data, the following dosage levels for the translocation study were selected.

Maximum dose	1200 mg/kg
Minimum dose	120 mg/kg

F₀ Generation

Although information about the F₀ generation should be included in the evaluation of translocation data, often it has not been presented or discussed in the reporting of a translocation study. Information on breeding performance of the mouse strain used, litter size or distribution, sex distribution, and the effect of compound treatment on the above, can provide valuable background data.

Table 16 summarizes the breeding and litter performance of the F₀ generation. The TEM I experiment produced a high degree of sterility. Therefore, it was necessary to reduce the concentration of TEM in an ongoing second experiment. By reducing TEM in the drinking water to one-third the original concentration, the second experiment provided

us with a satisfactory mutagenic response. No adverse effects were observed in either of the manganese sulfate ($MnSO_4$, FDA No. 71-71)-treated groups. Both control groups performed in a normal manner for this strain of mouse.

Table 17 presents litter-size distribution of the F_0 generation mice. Although litter sizes were smaller in the TEM-treated groups, other groups had normal litter-size distributions.

F_1 Generation

Table 18 summarizes breeding data for the F_1 generation mice. In the TEM I experiment, there was a decrease in the percentage of pregnancies. Other groups responded normally for the ICR/SIM mouse strain.

Litter-size distributions are presented in Table 19. As was the case with the F_0 generation, TEM groups had smaller litters. Other groups were normal.

Dead implants per F_1 male are presented in Table 20; dead implants per female are summarized in Table 21. In both TEM studies, there were greater numbers of females with 3 to 5 dead implants than in the control or $MnSO_4$ groups. Dead implant incidence for these latter groups was low and similar.

Table 22 presents a summary of the breeding results, by group, of those F_1 males found to be sterile or partially sterile. In Table 23, the individual F_1 animals are identified by number and treatment. TEM groups I and II showed an incidence of this response of 75% and 15%, respectively; the reference control and $MnSO_4$ groups had an incidence ranging from 1% to 3%. Females bred to partially sterile males in the TEM groups showed an increased number of dead implants along with a lesser number of viable implants. This condition was not seen in the reference control or $MnSO_4$ groups. Individual data on these animals can be found on the project "Translocation Data Sheets," which will be submitted separately to FDA.

Tables 24 to 26 present summary breeding and rebreeding data of presumptive F_1 males. In the first reference control experiment,

five males were nonbreeders and one met the criteria of "presumptive". When these animals were rebred, only two of these remained as nonbreeders. The second reference control experiment provided similar type responses. Out of 100 F₁ males in this group, six were found to be presumptive mutants after the first breeding schedule; the rebreeding of these males showed only one animal remaining as a presumptive. This male (No. 1455) had two females with seven viable implants per female and one female with plugs but no pregnancy; the rebreeding with three new females showed no evidence of mating (Table 24).

In Table 25, the effect of TEM producing heritable translocations is strongly implied. Eight F₁ males from the first TEM study produced six presumptive mutants by our evaluative criteria. Rebreading of these six a second and third time continued to show a presumptive mutant condition for all six animals. For the second TEM experiment with 112 F₁ males, 17 of these animals fit the criteria of "presumptive" after the first breeding schedule. When these 17 were rebred to new females, 14 of the males still remained as presumptive mutants.

For MnSO₄ (Table 26), 100 F₁ males (from the 120 ppm dietary treatment of the F₀ generation) showed four animals to be presumptive mutants after the first breeding. When these four were rebred, only one male still remained in the presumptive mutant category. This single animal showed no evidence of mating with any of its six females. For the 1200 ppm MnSO₄ group, three males out of the 100 tested showed no evidence of mating after the first breeding. When the three were rebred, all three animals demonstrated a normal response.

Cytogenetic Studies

Table 27 shows the findings from the cytogenetic evaluation of meiotic cell preparations from those F₁ males selected by the FDA project officer for examination. Dr. Lavappa found the two control I and one control II mice to be cytogenetically normal. The three TEM I mice, however, each had single reciprocal translocations. His report to SRI included the following statement:

These animals were examined for the heritable cytogenetic abnormalities (reciprocal translocations). Three of these animals F₁ 103, 106, and 108 each had single reciprocal translocations. The other three animals F₁ 15, 40, and 1455 were cytogenetically normal.

The original report by Dr. Lavappa and photographs are on file at Stanford Research Institute.

The main objective of this investigation was to study the methodology of performing mammalian translocation experiments and to evaluate such a procedure with a specific compound, MnSO₄. The original experimental plan involved a single breeding of F₁ males to virgin females. The results of this effort produced relatively large numbers of nonbreeder and partially sterile animals, as many as four to eight per group. Examination of the breeding data from these suspect animals showed many not to have had evidence of mating--no evidence of a vaginal plug in any of the three females caged with a specific male. Thus, it was decided to rebreed each of these suspect males to three additional virgin females. Although this extra task went beyond the requirements of this contract, it was our intent that this procedure be developed in a manner which would provide maximum information, still considering the realistic output of effort and cost.

We believe this rebreeding of initial presumptive mutant males is a significant contribution to reducing the possible interpretive error of presumptive mutant occurrence. For definitive confirmation of these biological results, cytogenetic examination of these animals should be done. Cytogenetic study of meiotic cells is tedious and time consuming. If confirmation of presumptive males had been done after the first breeding schedule was completed, some 42 animals would have had to have been examined. After the rebreeding regimen, only 24 animals still remained as presumptive mutants. These totals include the TEM groups as well as the reference control and MnSO₄ groups. If the TEM animals are excluded, there would have been 19 presumptive mutants in the reference control and MnSO₄ group after the first breeding;

when rebred, only 4 animals remained as presumptive mutants (3 controls and 1 in the 120 ppm MnSO₄ group).

Careful review and evaluation of the data do not show manganese sulfate (FDA No. 71-71) to be a mutagen in the mouse by the translocation test.

Table 1

**SUMMARY OF HOST-MEDIATED ASSAYS WITH
SALMONELLA TYPHIMURIUM TA1530**

The values are the averages for at least 7 mice.

<u>Regimen</u>	<u>Compound</u>	<u>Dose/kg</u>	<u>Average CFU/ml (x 10⁹)</u>	<u>Average His⁺ Revertants/ml</u>	<u>His⁺ Revertants/ 10⁸ CFU</u>
Single treatment	Negative control		1.77	148	8.3
	DMNA	100 mg	2.52	729	29.8
	Manganese sulfate	12 mg	1.70	144	8.6
		120 mg	1.48	107	7.3
		1200 mg	1.40	101	7.4
Multiple treatment (5 doses)	Negative control		0.94	77	8.6
	Manganese sulfate	12 mg	0.91	83	11.3
		120 mg	0.83	79	9.6
		1200 mg	0.86	111	14.8

Table 2

**SUMMARY OF HOST-MEDIATED ASSAYS WITH
SACCHAROYMICES CEREVIAE D3**

The values are the averages for at least 7 mice.

<u>Regimen</u>	<u>Compound</u>	<u>Dose/kg</u>	<u>Average CFU/ml (x 10⁷)</u>	<u>Average Ade Recombinants/ml</u>	<u>Ade Recombinants/10⁵ CFU</u>
Single treatment	Negative control		1.87	19	10.6
	EMS	350 mg	3.15	16.8	74.6
	Manganese sulfate	12 mg	2.10	2.3	12.4
		120 mg	2.30	1.2	5.8
		1200 mg	2.93	1.6	11.2
Multiple treatment (5 doses)	Negative control		1.48	1.3	5.9
	Manganese sulfate	12 mg	2.26	1.8	7.6
		120 mg	0.84	0.6	10.9
		1200 mg	2.36	1.3	9.0

Table 3
HOST-MEDIATED ASSAY WITH SALMONELLA TYPHIMURIUM TA1530

The mice were given a single oral dose of manganese sulfate. The positive control, DMNA, was given intramuscularly.

<u>Compound</u>	<u>Dose/kg</u>	<u>Mouse Number</u>	<u>CFU/ml (x 10⁹)</u>	<u>His⁺ Revertants/ml</u>	<u>His⁺ Revertants/10⁸ CFU</u>
Negative control		1	2.17	162	7.5
		2	1.45	117	8.1
		3	1.84	190	10.3
		4	1.67	151	9.0
		5	2.05	175	8.5
		6	1.53	126	8.2
		7	1.48	103	7.0
		8	2.00	157	7.9
		Average	1.77	148	8.3
DMNA (Positive control)	100 mg	1	5.45	1132	20.8
		2	1.33	257	19.3
		3	3.83	863	22.5
		4	2.85	1587	55.7
		5	1.67	468	28.0
		6	1.43	512	35.8
		7	1.07	283	26.4
		Average	2.52	729	29.8
Manganese sulfate	12 mg	1	1.63	128	7.9
		2	2.08	147	7.1
		3	0.97	103	10.6
		4	1.88	167	8.9
		5	1.67	214	12.8
		6	2.15	186	8.7
		7	1.88	145	7.7
		8	1.67	110	6.6
		9	1.33	95	7.1
		Average	1.70	144	8.6
120 mg	120 mg	1	0.67	53	7.9
		2	1.25	89	7.1
		3	1.41	78	5.5
		4	2.50	157	6.3
		5	1.53	89	5.8
		6	1.20	112	9.3
		7	1.83	168	9.2
Average			1.48	107	7.3

Table 3 (Concluded)

<u>Compound</u>	<u>Dose/kg</u>	<u>Mouse Number</u>	<u>CFU/ml (x 10⁹)</u>	<u>His⁺ Revertants/ ml</u>	<u>His⁺ Revertants/ 10⁸ CFU</u>
Manganese	1200 mg	1	1.09	93	8.5
		2	1.83	112	6.1
		3	2.16	140	6.5
		4	1.24	96	7.7
		5	1.33	110	8.3
		6	0.85	61	7.2
		7	1.27	95	7.5
Average			1.40	101	7.4

Table 4
HOST-MEDIATED ASSAY WITH SALMONELLA TYPHIMURIUM TA1530

The mice were given manganese sulfate at the doses indicated for five consecutive days.

<u>Compound</u>	<u>Dose/kg</u>	<u>Mouse Number</u>	<u>CFU/ml (x 10⁹)</u>	<u>His⁺ Revertants/ml</u>	<u>His⁺ Revertants/10⁸ CFU</u>
Negative control		1	0.79	59	7.5
		2	0.78	111	14.2
		3	0.84	78	9.3
		4	1.05	80	7.6
		5	0.68	60	8.8
		6	1.18	67	5.6
		7	1.25	87	7.0
		Average	0.94	77	8.6
Manganese sulfate	12 mg	1	0.34	89	26.0
		2	1.48	128	8.6
		3	0.86	48	5.6
		4	0.74	92	12.4
		5	0.52	70	13.5
		6	1.13	67	5.9
		7	1.33	90	6.8
		Average	0.91	83	11.3
	120 mg	1	0.66	98	14.8
		2	0.37	25	6.8
		3	0.72	53	7.4
		4	1.53	134	8.8
		5	0.45	38	8.3
		6	1.27	103	8.1
		7	0.67	72	10.7
		8	0.96	112	11.7
		Average	0.83	79	9.6
	1200 mg	1	0.85	91	10.7
		2	0.27	67	24.7
		3	0.84	139	16.5
		4	0.98	163	16.6
		5	1.27	138	10.9
		6	0.46	78	17.0
		7	1.38	103	7.5
		Average	0.86	111	14.8

Table 5
HOST-MEDIATED ASSAY WITH SACCHAROMYCES CEREVISIAE D3

The mice were given a single oral dose of manganese sulfate. The positive control, EMS, was given intramuscularly.

<u>Compound</u>	<u>Dose/kg</u>	<u>Mouse Number</u>	<u>CFU/ml (x 10⁷)</u>	<u>Ade Recombinants/ml (x 10³)</u>	<u>Ade Recombinants/10⁵ CFU</u>
Negative control		1	1.35	3.0	22.2
		2	1.78	2.0	11.2
		3	1.62	4.5	27.8
		4	3.28	3.0	9.1
		5	1.50	0.5	3.3
		6	2.23	1.0	4.5
		7	1.62	0.5	3.1
		8	1.58	0.5	3.2
		Average	1.87	1.9	10.6
EMS (Positive control)	350 mg	1	1.15	15.5	135.0
		2	3.70	27.5	74.0
		3	5.43	16.0	29.5
		4	4.35	12.0	27.6
		5	3.97	12.5	31.5
		6	0.98	14.0	143.0
		7	2.45	20.0	81.6
		Average	3.15	16.8	74.6
Manganese sulfate	12 mg	1	2.07	2.0	9.7
		2	0.49	0.5	10.2
		3	1.72	2.5	14.6
		4	2.58	1.5	5.8
		5	2.47	6.0	24.3
		6	0.47	1.0	21.4
		7	3.60	2.5	6.9
		8	2.02	2.0	9.9
		9	3.52	3.0	8.5
		Average	2.10	2.3	12.4
	120 mg	1	1.57	1.0	6.4
		2	3.68	1.5	4.1
		3	3.37	1.0	3.0
		4	0.78	0.5	6.4
		5	3.15	1.5	4.8
		6	3.02	3.0	9.9
		7	0.54	0	
		Average	2.30	1.2	5.8

Table 5 (Concluded)

<u>Compound</u>	<u>Dose/kg</u>	<u>Mouse Number</u>	<u>CFU/ml (x 10⁷)</u>	<u>Ade⁻ Recombinants/ ml (x 10³)</u>	<u>Ade⁻ Recombinants/ 10⁵ CFU</u>
Manganese sulfate	1200 mg	1	6.60	5.5	8.3
		2	4.63	1.0	2.2
		3	0.56	0.5	8.7
		4	1.54	3.5	22.7
		5	1.39	2.0	14.4
		6	1.43	2.5	17.5
		7	4.33	2.0	4.6
Average			2.93	1.6	11.2

Table 6
HOST-MEDIATED ASSAY WITH SACCHAROMYCES CEREVISIAE D3

The mice were given manganese sulfate at the doses indicated for five consecutive days.

<u>Compound</u>	<u>Dose/kg</u>	<u>Mouse Number</u>	<u>CFU/ml (x 10⁷)</u>	<u>Ade Recombinants/ml (x 10³)</u>	<u>Ade Recombinants/10⁵ CFU</u>
Negative control		1	1.60	0.5	3.1
		2	4.10	3.5	8.5
		3	2.17	2.0	9.2
		4	2.17	1.5	6.9
		5	1.38	1.0	7.2
		6	0.84	0.5	6.0
		7	1.37	0.5	3.6
		8	1.87	0.5	2.7
		Average	1.48	1.3	5.9
Manganese sulfate	12 mg	1	2.61	3.0	11.5
		2	2.50	2.5	10.0
		3	2.50	1.5	6.0
		4	2.35	1.0	4.3
		5	1.48	0.5	3.4
		6	3.20	3.0	9.4
		7	1.75	1.0	5.7
		8	2.50	2.0	8.0
		9	1.48	1.5	10.1
		Average	2.26	1.8	7.6
	120 mg	1	0.35	0.5	14.4
		2	1.18	0.5	4.2
		3	0.62	1.5	24.3
		4	1.01	0.5	4.9
		5	0.21	0.5	24.0
		6	0.28		
		7	2.20	1.0	4.5
		Average	0.84	0.6	10.9
	1200 mg	1	0.98	1.0	10.2
		2	2.33	1.5	6.4
		3	5.78	2.0	5.5
		4	3.08	1.5	4.9
		5	2.08	0.5	2.4
		6	1.38	1.5	10.8
		7	0.86	1.0	11.6
		Average	2.36	1.3	9.0

Table 7
IN VITRO ASSAYS OF MANGANESE SULFATE WITH FOUR STRAINS OF SALMONELLA TYPHIUMURIUM

Experiment Number	Compound	Amount Added/Plate	Metabolic Activation	<u>His</u> ⁺ Revertants per Plate				
				TA1530	TA1535	TA1536	TA1537	TA1538
1	Negative control		-		19	2	22	16
	2-Fluorenamine	5 µg	-					31
36	Manganese sulfate	100 mg	-	24	0	9	17	
			+	7	1	10	17	
2	Negative control		-		10			4
			+		22			7
3	N-Methyl-N'-nitro-N-nitroso guanidine (crystal added to center of plate)		-		+*			-*
			+		+			-
36	Ethyl methane sulfonate (10 µl added to 6 mm sterile filter disc)		-		+			-
			+		+			-
36	Dimethylnitrosamine (10 µl added to 6 mm sterile filter disc)		-		-			-
			+		+			-
36	Manganese sulfate	100 mg	-		8			11
			+		10			1

*+ indicates a ring of mutants around the spot where the chemical was added.

- indicates no ring of mutants.

Table 8
IN VITRO ASSAY OF MANGANESE SULFATE WITH SACCHAROMYCES CEREVISIAE D3

<u>Compound</u>	<u>Percent Concentration (w/v or v/v)</u>	<u>CFU/ml (x 10⁷)</u>	<u>Ade- Recombinants/ml (x 10³)</u>	<u>Percent Survivors</u>	<u>Ade Recombinants/ 10⁵ CFU</u>
Negative control		8.17	4.5	100%	5.1
EMS (Positive control)	1%	4.80	119.0	59	248.0
Manganese sulfate	5	6.25	3.5	76	5.6

A minimum of 120,000 colonies were scanned for mitotic recombinants.

DOMINANT LETHAL STUDY - RAT

TABLE 9

AVERAGE IMPLANTATIONS PER PREGNANT FEMALE

WEEK	CONTROL	71-71		12 MG/KG		71-71		120 MG/KG		71-71		1200 MG/KG		TEM	12 MG/KG	
		71-71	12 MG/KG	71-71	120 MG/KG	71-71	1200 MG/KG	71-71	1200 MG/KG	71-71	1200 MG/KG	71-71	1200 MG/KG			
SINGLE TREATMENT																
38	1 177/ 15=11.60	232/ 20=11.60		176/ 16=11.00		227/ 19=11.95		201/ 17=11.82								
	2 214/ 20=10.70	215/ 19=11.32		175/ 16=10.94		232/ 20=11.60		202/ <0=10.10								
	3 245/ 20=12.25	246/ 20=12.30		200/ 18=11.11		225/ 20=11.25		147/ <0= 7.35 **								
	4 237/ 20=11.85	241/ 20=12.05		261/ 20=13.05		243/ 20=12.15		103/ 17= 6.06 **								
	5 246/ 20=12.30	251/ 20=12.55		249/ 20=12.45		228/ 19=12.00		226/ 20=11.30								
	6 230/ 20=11.50	229/ 20=11.45		229/ 20=11.45		239/ 20=11.95		253/ 20=12.65 *I								
	7 226/ 20=11.30	250/ 20=12.50		241/ 20=12.05		238/ 20=11.90		261/ 20=13.05								
	8 249/ 20=12.45	257/ 20=12.85		241/ 20=12.05		252/ 20=12.60		247/ 20=12.35								
MULTIPLE TREATMENT																
	1 223/ 20=11.15	199/ 18=11.06		176/ 16=11.00		209/ 17=12.29										
	2 249/ 20=12.45	194/ 17=11.41		224/ 19=11.79		259/ 20=12.95										
	3 235/ 20=11.75	212/ 17=12.47		239/ 20=11.95		236/ 20=11.80										
	4 268/ 20=12.40	224/ 18=12.44		247/ 20=12.35		249/ 19=13.11										
	5 214/ 18=11.89	201/ 18=11.17		227/ 20=11.35		255/ 20=12.75										
	6 246/ 20=12.20	230/ 17=13.53 *I		250/ 19=13.16		231/ 18=12.83										
	7 237/ 20=11.85	198/ 16=12.37		238/ 20=11.90		239/ 20=11.95										

* SIGNIFICANT AT P LT .05

** SIGNIFICANT AT P LT .01

I INCREASED ABOVE CONTROL

DOMINANT LETHAL STUDY - RAT

TABLE 10

AVERAGE DEAD IMPLANTS PER PREGNANT FEMALE

WEEK	CONTROL	71-71		12 MG/KG		71-71		120 MG/KG		71-71		1200 MG/KG		ITEM	12 MG/KG	COMPOUND FIDA NO	MANGANESE SULFATE 71-71	
		71-71	12 MG/KG	71-71	120 MG/KG	71-71	1200 MG/KG	71-71	1200 MG/KG	71-71	1200 MG/KG	71-71	1200 MG/KG					
SINGLE TREATMENT																		
39	1	6/	15± .4-	7/	20± .35	15/	16± .94	10/	19± .53	55/	17± 3.24 **							
	2	8/	20± .40	14/	19± .74	10/	16± .63	13/	20± .65	133/	20± 6.65 **							
	3	16/	20± .80	16/	20± .80	14/	18± .78	7/	21± .35	119/	20± 5.45 **							
	4	9/	20± .45	21/	20± 1.05	17/	20± .85	16/	20± .60	96/	17± 5.41 **							
	5	24/	20± 1.20	22/	20± 1.10	13/	20± .65	26/	19± 1.37	60/	20± 3.00 **							
	6	15/	20± .75	11/	20± .55	7/	20± .35	11/	20± .55	7/	20± .35							
	7	7/	20± .35	12/	20± .60	13/	20± .65	14/	20± .70	14/	20± .70							
	8	23/	20± 1.15	16/	20± .90	17/	20± .65	12/	20± .60	16/	20± .60							
MULTIPLE TREATMENT																		
	1	35/	20± 1.75	16/	18± .89	13/	16± .81	10/	17± .59 *D									
	2	22/	20± 1.1*	21/	17± 1.24	11/	19± .58	20/	20± 1.00									
	3	18/	20± .90	28/	17± 1.65	26/	20± 1.30	6/	20± .30									
	4	29/	20± 1.45	30/	18± 1.67	16/	20± .80	13/	19± .68									
	5	15/	18± .83	26/	18± 1.44	22/	20± 1.10	20/	20± 1.00									
	6	10/	20± .50	8/	17± .47	13/	19± .68	6/	18± .44									
	7	21/	20± 1.05	16/	16± 1.00	11/	20± .55	5/	20± .25 *D									

* SIGNIFICANT AT P LT 0.05

** SIGNIFICANT AT P LT (.01)

D DECREASED BELOW CONTROL

DOMINANT LETHAL STUDY - RAT

TABLE 11

LEAD IMPLANTS/TOTAL IMPLANTS

WEEK	CONTROL	71-71		120 MG/KG		71-71		1200 MG/KG		TEM	12 MG/KG
		FDA NO	MANGANESE SULFATE	FDA NO	MANGANESE SULFATE	FDA NO	MANGANESE SULFATE	FDA NO	MANGANESE SULFATE		
SINGLE TREATMENT											
1	6/ 172= .03	7/ 232= .03	15/ 176= .09	10/ 227= .04	55/ 201= .27**						
2	8/ 214= .04	14/ 215= .07	10/ 175= .06	13/ 232= .06	133/ 202= .66**						
3	16/ 245= .07	16/ 246= .07	14/ 200= .07	7/ 225= .03	119/ 147= .51**						
4	9/ 237= .04	21/ 241= .09	17/ 261= .07	16/ 243= .07	92/ 103= .59**						
5	24/ 246= .1*	22/ 251= .09	13/ 249= .05	26/ 228= .11	60/ 226= .27**						
6	15/ 230= .07	11/ 229= .05	7/ 229= .03	11/ 239= .05	7/ 253= .03*D						
7	7/ 226= .03	12/ 250= .05	13/ 241= .05	14/ 238= .06	14/ 261= .05						
8	23/ 244= .09	18/ 257= .07	17/ 241= .07	12/ 252= .05	18/ 247= .07						
MULTIPLE TREATMENT											
1	35/ 223= .16	16/ 199= .08	13/ 170= .07	10/ 209= .05*D							
2	22/ 249= .09	21/ 194= .11	11/ 224= .05	20/ 259= .08							
3	14/ 235= .08	28/ 212= .13	26/ 239= .11	6/ 236= .03							
4	29/ 248= .12	30/ 224= .13	16/ 247= .06	13/ 249= .05							
5	15/ 214= .07	26/ 201= .13	22/ 227= .10	20/ 255= .04							
6	16/ 244= .04	8/ 230= .03	13/ 250= .05	8/ 231= .03							
7	21/ 231= .09	16/ 198= .08	11/ 238= .05	5/ 239= .02*D							

* SIGNIFICANT AT P LT 0.05

** SIGNIFICANT AT P LT 0.01

D DECREASED BELOW CONTROL

DOMINANT LETHAL STUDY - RAT

TABLE 12
AVERAGE CORPORA LUTEA PER PREGNANT FEMALE

WEEK	LUNTHUL	71-71		120 MG/KG		71-71		1200 MG/KG		ITEM		12 MG/KG	
		FDA NO	CUMPOUND	FDA NO	CUMPOUND	FDA NO	CUMPOUND	FDA NO	CUMPOUND	FDA NO	CUMPOUND	FDA NO	CUMPOUND
SINGLE TREATMENT													
1	194/ 15=12.93	261/ 20=13.05		215/ 16=13.44		264/ 19=12.84		226/ 17=13.29					
2	245/ 20=12.25	238/ 19=12.53		195/ 16=12.19		246/ 20=12.30		255/ 20=12.75					
3	256/ 20=12.80	265/ 20=13.25		231/ 16=12.83		241/ 20=12.05		221/ 20=11.05 **					
4	250/ 20=12.50	253/ 20=12.65		279/ 20=13.95*		253/ 20=12.65		205/ 17=12.06					
5	274/ 20=13.70	262/ 20=13.10		293/ 20=14.65		245/ 19=12.69		250/ 20=12.50 *					
6	250/ 20=12.50	278/ 20=13.90 *		260/ 20=13.00		266/ 20=13.30		265/ 20=13.25					
7	262/ 20=13.10	277/ 20=13.85		263/ 20=13.15		267/ 20=13.35		274/ 20=13.70					
8	254/ 20=12.90	270/ 20=13.50		269/ 20=13.45		272/ 20=13.60		269/ 20=13.45					
MULTIPLE TREATMENT													
1	254/ 20=12.70	233/ 18=12.94		199/ 16=12.44		220/ 17=12.94							
2	265/ 20=13.25	209/ 17=12.29 *		255/ 19=13.42		278/ 20=13.90							
3	256/ 20=12.80	221/ 17=13.00		257/ 20=12.85		269/ 20=13.45							
4	296/ 20=14.80	269/ 18=14.94		271/ 20=13.85		262/ 19=13.79							
5	258/ 16=14.33	242/ 18=13.44		274/ 20=13.70		279/ 20=13.95							
6	266/ 20=13.30	247/ 17=14.53 *		258/ 19=13.58		261/ 16=14.50							
7	260/ 20=13.00	214/ 16=13.37		260/ 20=13.00		276/ 20=13.60							

* SIGNIFICANT AT P LT 0.05

** SIGNIFICANT AT P LT 0.01

DOMINANT LETHAL STUDY - RAT

TABLE 13
AVERAGE PREIMPLANTATION LOSS PER PREGNANT FEMALE

WEEK	CONTROL	71-71		12 MG/KG		71-71		120 MG/KG		71-71		1200 MG/KG		ITEM	+2 MG/KG
		FDA NO	MANGANESE SULFATE	FDA NO	MANGANESE SULFATE	FDA NO	MANGANESE SULFATE	FDA NO	MANGANESE SULFATE	FDA NO	MANGANESE SULFATE	FDA NO	MANGANESE SULFATE		
SINGLE TREATMENT															
1	17/ 15± 1.13	29/ 20± 1.45		39/ 16± 2.44		17/ 19± .84		25/ 17± 1.47							
2	31/ 20± 1.55	23/ 19± 1.21		20/ 16± 1.25		14/ 20± .70		53/ 20± 2.65 *							
3	11/ 20± .55	19/ 20± .95		31/ 18± 1.72 *		16/ 20± .80		74/ 20± 3.10 **							
4	13/ 20± .65	12/ 20± .60		18/ 20± .90		10/ 20± .50		102/ 17± 6.00 **							
5	28/ 20± 1.40	11/ 20± .55		44/ 20± 2.20		17/ 19± .84		24/ 20± 1.20							
6	20/ 20± 1.00	49/ 20± 2.45		31/ 20± 1.55		27/ 20± 1.35		12/ 20± .60							
7	36/ 20± 1.80	27/ 20± 1.35		22/ 20± 1.10		29/ 20± 1.45		13/ 20± .65							
8	9/ 20± .45	13/ 20± .65		28/ 20± 1.40		20/ 20± 1.00		22/ 20± 1.10							
MULTIPLE TREATMENT															
1	31/ 20± 1.55	34/ 18± 1.49		23/ 16± 1.44		11/ 17± .65									
2	16/ 20± .80	15/ 17± .68		31/ 19± 1.63 *		19/ 20± .95									
3	21/ 20± 1.05	9/ 17± .53		18/ 20± .90		33/ 20± 1.65									
4	48/ 20± 2.40	45/ 18± 2.50		30/ 20± 1.50		13/ 19± .68 *D									
5	44/ 18± 2.44	41/ 18± 2.28		47/ 20± 2.35		24/ 20± 1.20									
6	22/ 20± 1.10	17/ 17± 1.00		8/ 19± .42		30/ 18± 1.67									
7	23/ 20± 1.15	16/ 16± 1.00		22/ 20± 1.10		37/ 20± 1.65									

* SIGNIFICANT AT P LT 0.05

** SIGNIFICANT AT P LT 0.01

D DECREASED BELOW CONTROL

DOMINANT LETHAL STUDY OF COMPOUND 71-71

MANGANESE SULFATE

TABLE 14
CHI-SQUARE TEST OF THE FERTILITY INDEX (1 DEGREE OF FREEDOM)

WEEK	VEHICLE CONTROL				71-71 12 MG/KG				71-71 120 MG/KG				71-71 1200 MG/KG				TEM		+2 MG/KG		
	N	N	FERT.	CHISU	N	N	FERT.	CHISU	N	N	FERT.	CHISQ	N	N	FERT.	CHISU	N	N	FERT.	CHISU	
	PRG	MTR	INDEX		PRG	MTR	INDEX		PRG	MTR	INDEX		PRG	MTR	INDEX		PRG	MTR	INDEX		
SINGLE TREATMENT																					
1	14	20	.75	0.00	20	20	1.00	3.66	16	20	.80	0.00	19	20	.95	1.76	17	20	.85	.16	
2	20	20	1.00	0.00	19	20	.95	0.00	16	20	.80	2.50	20	20	1.00	0.00	20	20	1.00	0.00	
3	20	20	1.00	0.00	20	20	1.00	0.00	18	20	.90	.53	20	20	1.00	0.00	20	20	1.00	0.00	
4	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	17	20	.85	1.44	
5	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	19	20	.95	0.00	20	20	1.00	0.00	
6	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	
7	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	
8	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	20	20	1.00	0.00	
MULTIPLE TREATMENT																					
1	20	20	1.00	0.00	18	20	.90	.53	16	20	.80	2.50	17	20	.85	1.44					
2	20	20	1.00	0.00	17	18	.94	0.00	19	20	.95	0.00	20	20	1.00	0.00					
3	20	20	1.00	0.00	17	18	.94	0.00	20	20	1.00	0.00	20	20	1.00	0.00					
4	20	20	1.00	0.00	18	18	1.00	0.00	20	20	1.00	0.00	19	20	.95	0.00					
5	18	20	.90	0.00	18	18	1.00	.42	20	20	1.00	.53	20	20	1.00	.53					
6	20	20	1.00	0.00	17	18	.94	0.00	19	20	.95	0.00	18	20	.90	.53					
7	20	20	1.00	0.00	16	18	.89	.65	20	20	1.00	0.00	20	20	1.00	0.00					

DOMINANT LETHAL STUDY OF COMPOUND 71-71 MANGANESE SULFATE

TABLE 15
CHI-SQUARE TEST OF THE DEATH INDEX (1 DEGREE OF FREEDOM)

WEEK	VPHILLIP CONTROL				71-71 12 MG/KG				71-71 120 MG/KG				71-71 1200 MG/KG				TEM 2 MG/KG			
	N WDI	N PRG	DEATH INDEX	CHISQ	N WDI	N PRG	DEATH INDEX	CHISQ	N WDI	N PRG	DEATH INDEX	CHISQ	N WDI	N PRG	DEATH INDEX	CHISQ	N WDI	N PRG	DEATH INDEX	CHISQ
SINGLE TREATMENT																				
1	4	15	.27	0.00	7	20	.35	.02	8	16	.50	.93	4	19	.21	.00	13	17	.76	.006*
2	5	20	.25	0.00	8	19	.42	.63	7	16	.44	.69	9	20	.45	.99	16	20	.80	10.03**
3	7	20	.35	0.00	10	20	.50	.41	8	18	.44	.07	6	20	.30	0.00	18	20	.90	10.67**
4	8	20	.40	0.00	12	20	.60	.90	10	20	.50	.10	7	20	.35	0.00	17	17	1.00	12.48**
5	11	20	.55	0.00	9	20	.45	.10	10	20	.50	0.00	12	19	.63	.04	16	20	.80	1.82
6	11	20	.55	0.00	6	20	.30	1.64	6	20	.30	1.64	6	20	.30	1.64	5	20	.25	2.60
7	7	20	.35	0.00	8	20	.40	0.00	8	20	.40	0.00	6	20	.30	0.00	10	20	.50	.41
8	10	20	.50	0.00	9	20	.45	0.00	9	20	.45	0.00	9	20	.45	0.00	10	20	.50	.10
MULTIPLE TREATMENT																				
1	15	20	.75	0.00	8	18	.44	2.53	7	16	.44	2.46	7	17	.41	3.07				
2	13	21	.65	0.00	7	17	.41	1.25	8	19	.42	1.24	9	20	.45	.91				
3	8	20	.40	0.00	12	17	.71	2.34	14	20	.70	2.53	6	20	.30	.11				
4	12	20	.60	0.00	11	18	.61	.07	10	20	.50	.10	9	19	.47	.22				
5	8	18	.44	0.00	10	18	.56	.11	10	20	.50	0.00	11	20	.55	.11				
6	6	20	.30	0.00	4	17	.24	.00	9	19	.47	.62	8	18	.44	.34				
7	9	20	.45	0.00	6	16	.38	.01	10	20	.50	0.00	3	20	.15	2.98				

* SIGNIFICANT AT PLT 0.05

** SIGNIFICANT AT PLT 0.01

Table 16

MnSO₄ TRANSLOCATION STUDY--SUMMARY OF BREEDING AND LITTER DATA
 F₀ GENERATION MICE

Parameter	Control I	Control II	TEM ^a I (0.32 mg/l--4 wks)	TEM ^a II (0.32 mg/l--2 wks) (0.12 mg/l--2 wks)	MnSO ₄ ^b (120 ppm)	MnSO ₄ ^b (1200 ppm)
Number of F ₀ males	40	40	40	60	39	39
Number of F ₀ females	81	80	81	180	78	78
Number pregnant	71	69	11	150	66	73
Percent pregnant	88	86	14	83	85	94
Number of nonbreeder males	1	2	31	3	2	0
Percent nonbreeders	2.5	5.0	77.5	5.0	5.1	0
Average litter size	10.0	10.20	2.36	7.24	9.81	9.94
Average number males/litter	5.15	5.39	0.73	3.71	4.67	4.71
Average number females/litter	4.77	4.81	1.45	3.53	5.07	4.68

^aTriethylenemelamine (TEM)

^bManganese sulfate (MnSO₄)

Table 17

MnSO₄ TRANSLOCATION STUDY--MOUSE LITTER SIZE DISTRIBUTION OF YOUNG DERIVED FROM F₀ GENERATION ADULTS

<u>Litter Size</u>	<u>Control I</u>	<u>Control II</u>	<u>TEM^a I (0.32 mg/l--4 wks)</u>	<u>TEM^a II (0.32 mg/l--2 wks)</u>	<u>MnSO₄^b (120 ppm)</u>	<u>MnSO₄^b (1200 ppm)</u>
1	0	0	2	2	1	0
2	0	0	1	3	0	0
3	0	0	0	3	1	2
4	0	3	1	9	0	1
5	1	2	1	10	0	1
6	4	0	1	16	0	2
7	5	0	1	29	3	0
8	6	3	0	19	7	4
9	8	8	0	23	16	14
10	15	21	0	16	8	20
11	13	15	0	6	15	14
12	9	12	0	6	6	10
13	3	3	0	1	6	4
14	4	2	0	1	1	0
15	2	0	0	0	1	1
16	0	0	0	0	0	0
17	0	0	0	0	0	0
18	0	0	0	0	0	0
Mean (μ)	10.14	10.20	3.71	7.54	9.98	9.94
Variance (σ^2)	5.14	4.37	5.83	6.13	5.23	4.67
Standard deviation (σ)	2.27	2.09	2.41	2.48	2.29	2.16

^aTriethylenemelamine (TEM)

^bManganese sulfate (MnSO₄)

Table 18

MnSO₄ TRANSLOCATION STUDY--MOUSE SUMMARY BREEDING DATA OF F₁ GENERATION

Parameter	Control I	Control II	TEM ^a I (0.32 mg/1--4 wks)	TEM ^a II (0.32 mg/1--2 wks) (0.12 mg/1--2 wks)	MnSO ₄ ^b (120 ppm)	MnSO ₄ ^b (1200 ppm)
Number of F ₁ males	97	100	8	112	100	100
Number of F ₁ females	297	300	24	336	300	300
Number of mating plugs	244	267	16	281	273	275
Percent mating plugs	82	89	67	84	91	92
Number of pregnant females	256	242	13	268	271	270
Percent pregnant	86	81	54	80	90	90
Number pregnant with mating plugs	240	240	12	257	265	263
Percent pregnant with mating plugs	94	99	92	96	88	88
Number pregnant without mating plugs	16	2	1	11	7	7
Percent pregnant without mating plugs	6	1	8	4	2	2
Number of females not pregnant	41	58	11	68	29	30
Percent females not pregnant	14	19	46	20	10	10
Number not pregnant with mating plugs	4	27	4	24	8	12
Percent not pregnant with mating plugs	10	46	36	35	3	4
Nonbreeder and sterile males	5	0	2	3	2	3
Percent nonbreeder and sterile males	5	0	25	3	2	3

^aTriethylenemelamine (TEM)^bManganese sulfate (MnSO₄)

Table 19
 $MnSO_4$ TRANSLOCATION STUDY--MOUSE LITTER SIZE DISTRIBUTION OF YOUNG DERIVED FROM F₁ GENERATION ADULTS

Litter Size	Control I	Control II	TEM ^{a,b} I (0.32 mg/l--4 wks)	TEM ^a II (0.32 mg/l--2 wks) (0.12 mg/l--2 wks)	$MnSO_4$ ^c (120 ppm)	$MnSO_4$ ^c (1200 ppm)
1	0	1	4	4	0	0
2	1	2	3	6	2	2
3	1	1	2	6	2	1
4	3	3	8	6	0	1
5	2	4	4	10	2	2
6	1	2	4	5	4	3
7	6	7	1	5	12	7
8	7	16	1	14	16	15
9	24	31	1	36	57	40
10	35	49	2	70	51	66
11	49	45	4	41	61	56
12	62	48	4	36	34	48
13	41	21	0	19	22	25
14	14	6	0	5	7	1
15	8	3	0	1	1	3
16	2	1	0	1	0	0
17	0	1	0	0	0	0
18	0	1	0	0	0	0
Mean (μ)	11.18	10.42	6.0	9.58	10.17	10.39
Variance (σ^2)	4.71	5.64	13.30	8.10	4.05	3.71
Standard deviation (σ)	2.17	2.37	3.65	2.85	2.01	1.93

^aTriethylenemelamine (TEM)

^bTotal of three matings--9 females per male--8 males.

^cManganese sulfate ($MnSO_4$)

Table 20

 MnSO_4 TRANSLOCATION STUDY--SUMMARY OF DEAD IMPLANT OCCURRENCE PER F_1 MALE MOUSE

Parameter	Control I	Control II	TEM ^a I (0.32 mg/1--4 wks)	TEM ^a II (0.32 mg/1--2 wks)	MnSO_4 ^b (120 ppm)	MnSO_4 ^b (1200 ppm)
Number of F_1 males	99	100	8	112	100	100
♂'s having ♀s with no dead implants	35	40	1	36	31	44
♂'s having ♀s with 1 dead implant	29	32	1	41	28	25
♂'s having ♀s with 2 dead implants	18	17	0	10	24	16
♂'s having ♀s with 3 dead implants	7	5	0	6	7	7
♂'s having ♀s with 4 dead implants	2	6	0	4	5	4
♂'s having ♀s with 5 dead implants	2	0	0	0	3	0
♂'s having ♀s with more than 5 dead implants	1	0	4	12	0	1

^aTriethylenemelamine (TEM)^bManganese sulfate (MnSO_4)

Table 21

MnSO₄ TRANSLOCATION STUDY--SUMMARY OF DEAD IMPLANTS PER PREGNANT FEMALE
(FIRST BREEDING OF FEMALES TO F₁ MALES)

Parameter	Control I	Control II	TEM ^a I (0.32 mg/l--4 wks)	TEM ^a II (0.32 mg/l--2 wks) (0.12 mg/l--2 wks)	MnSO ₄ ^b (120 ppm)	MnSO ₄ ^b (1200 ppm)
Number of pregnant females	256	242	13	268	271	270
?s with no dead implants	175	160	3	160	174	196
?s with 1 dead implant	61	62	1	64	68	53
?s with 2 dead implants	14	17	0	14	24	17
?s with 3 dead implants	4	3	0	7	4	3
?s with 4 dead implants	1	0	3	5	1	1
?s with 5 dead implants	1	0	0	1	0	0
50 ?s with more than 5 dead implants	0	0	6	17	0	0

Table 22
MnSO₄ TRANSLOCATION STUDY--SUMMARY OF PRESUMPTIVE TRANSLOCATION F₁ MALES AFTER TWO BREEDINGS

Parameter	Control I	Control II	TEM ^a I (0.32 mg/l--4 wks)	TEM ^a II (0.32 mg/l--2 wks) (0.12 mg/l--2 wks)	MnSO ₄ ^b (120 ppm)	MnSO ₄ ^b (1200 ppm)
Total number of F ₁ males	99	100	8	112	100	100
Number of nonbreeder males	2	0	1	0	1	0
Number of presumptive sterile males	0	0	0	3	0	0
Number of partially sterile males	0	1	5	11	0	0

^aTriethylenemelamine (TEM)

^bManganese sulfate (MnSO₄)

Table 23

MnSO₄ TRANSLOCATION STUDY--INDIVIDUAL IDENTIFICATION OF NONBREEDER, PRESUMPTIVE STERILE,
AND PARTIALLY STERILE F₁ MALES AFTER TWO BREEDINGS

<u>Control I</u>	<u>Control II</u>	<u>TEM^a I (0.32 mg/l--4 wks)</u>	<u>TEM^a II (0.32 mg/l--2 wks)</u>	<u>MnSO₄^b (120 ppm)</u>	<u>MnSO₄^b (1200 ppm)</u>
<u>NON-BREEDER</u>					
15		102			939
40					
<u>PRESUMPTIVE STERILE</u>					
			1504		
			1546		
			1590		
<u>PARTIALLY STERILE</u>					
	1455	101	1515		
		103	1528		
		106	1544		
		107	1561		
		108	1565		
			1571		
			1572		
			1595		
			1602		
			1605		
			1612		

^aTriethylenemelamine (TEM)

^bManganese sulfate (MnSO₄)

Table 24

MnSO₄ TRANSLOCATION STUDY--BREEDING AND REBREEDING SUMMARY OF NONBREEDER
AND PRESUMPTIVE TRANSLOCATION F₁ MALES--CONTROLS

Treatment Group	F ₁ Male Number	First Breeding (3 females)			Second Breeding (3 females)		
Control I	15	-*	-	-	-	-	-
	16	-	-	-	10	-	-
	40	-	-	-	-	-	-
	41	-	-	-	10	-	-
	69	-	-	-	11	12	11
	77	6	4	8	7	11	-
Totals					2		
Control II	1403	0**	9	0	9	-	-
	1423	0	0	9	10	11	11
	1455	0	7	7	-	-	-
	1484	0	9	9	-	-	8
	1491	0	9	-	10	12	10
	1495	2	5	0	12	10	2
Totals					1		

* - indicates a plug was not detected and female was not pregnant.

**0 indicates a plug was observed but female was not pregnant.

Table 25

MnSO₄ TRANSLOCATION STUDY--BREEDING AND REBREEDING SUMMARY OF NONBREEDER
AND PRESUMPTIVE TRANSLOCATION F₁ MALES--POSITIVE CONTROLS

Treatment Group	F ₁ Male Number	First Breeding (3 females)			Second Breeding (3 females)			Third Breeding (3 females)			
TEM I (0.32 mg/l for 4 weeks)	101	0	**0	0	0	4	-	*	4	1	6
	102	-	-	-	-	-	-	-	-	-	-
	103	-	1	-	5	5	0	4	4	2	
	106	4	5	3	0	4	7	6	5	6	
	107	0	-	-	1	-	-	-	-	-	
	108	2	8	6	4	4	1	0	2	-	
Totals		6			6			6			
TEM II (0.32 mg/l for 2 weeks, 0.12 mg/l for 2 weeks)	1504	0	0	-	0	0	0				
	1515	3	3	4	5	4	2				
	1528	0	2	0	0	1	-				
	1544	4	2	1	3	0	5				
	1546	0	0	0	0	0	-				
	1551	0	-	-	0	12	10				
	1561	4	3	-	4	3	3				
	1565	0	4	2	4	2	1				
	1571	1	6	8	3	3	4				
	1572	5	2	6	-	-	-				
	1576	9	5	6	8	8	-				
	1590	0	0	0	0	0	0				
	1595	5	2	3	2	3	-				
	1599	9	4	-	12	12	-				
	1602	3	0	6	2	0	7				
	1605	5	0	2	-	-	-				
	1612	5	3	-	0	3	4				
Totals		17			14						

* - indicates a plug was not detected and female was not pregnant.

**0 indicates a plug was observed but female was not pregnant.

Table 26

MnSO₄ TRANSLOCATION STUDY--BREEDING AND REBREEDING SUMMARY
OF NONBREEDER AND PRESUMPTIVE TRANSLOCATION F₁ MALES--MnSO₄

<u>Treatment Group</u>	<u>F₁ Male Number</u>	<u>First Breeding (3 Females)</u>			<u>Second Breeding (3 Females)</u>		
MnSO ₄ (120 ppm)	909	- *	-	-	-	-	9
	914	9	6	7	3	-	12
	939	-	-	-	-	-	-
	994	<u>9</u>	<u>3</u>	<u>0</u> **	<u>9</u>	<u>11</u>	<u>10</u>
Totals		4			1		
MnSO ₄ (1200 ppm)	827	-	-	-	-	11	-
	866	-	-	-	12	9	-
	892	-	-	-	<u>10</u>	<u>11</u>	<u>10</u>
Totals		3			0		

* - indicates a plug was not detected and female was not pregnant.

** 0 indicates a plug was observed but female was not pregnant.

Table 27

MnSO₄ TRANSLOCATION STUDY--CYTOGENETIC EVALUATION
OF MEIOTIC CELLS FROM TESTES PREPARATIONS OF F₁ MICE

<u>Treatment</u>	<u>F₁ Male Number</u>	<u>Testes Weight (mg)</u>	<u>Classification After Two Breedings</u>	<u>Cytogenetic Classification</u>
Control I	15	272	Nonbreeder	Normal
	40	272	Nonbreeder	Normal
Control II	1455	301	Partially sterile	Normal
TEM I	103	375	Partially sterile	Positive reciprocal translocation
	106	259	Partially sterile	Positive reciprocal translocation
	108	252	Partially sterile	Positive reciprocal translocation

APPENDIX A

**STATISTICAL PROCEDURE FOR EVALUATION OF
DOMINANT LETHAL DATA WITH A DESCRIPTION
AND EXPLANATION OF THE COMPUTER PRINTOUTS**

Program Abstract

1. Serial Number: KSH009

2. Title: Chemical Mutagenicity Study

3. Deck Name: KLUTE

4. Abstract: This program performs statistical calculations to determine the mutagenicity of certain chemical compounds.

5. Originator: Jim Eusebio
June 1972

6. Revised: Kathleen S. Himmelberger

7. Date: February 8, 1974

8. Memory Requirements: 134236₈

9. Input: Data deck

10. Output: Printed output listing input data and results of several statistical tests (CHI-SQUARE test, ARMITAGE test, T-test, regression fits, PROBIT analysis, analysis of variance).

11. System: CDC 6400 Scope 3.3
FORTRAN IV

Program Description

The program which performs statistical calculations using the autopsy data of female rats is called KLUTE. KLUTE is written in FORTRAN IV for use on the CDC 6400. Because storage requirements of the program exceeded available memory, it was necessary to use overlays (see SCOPE Reference Manual, 6000 Version 3.3, pp 6-14 to 6-18). Therefore, card decks must be loaded in a specific order.

Although KLUTE was designed to allow as much flexibility in experimentation as possible, there are some criteria which must be satisfied:

1. The maximum number of test groups is included in the first week. After the first week, groups may be terminated. (Some studies mate the single-dose groups for eight weeks and multiple-dose groups for only seven.)
2. There are at most five single-dose groups and five multiple-dose groups. The program will handle experiments using only single-dose groups or multiple-dose groups.
3. A control group exists for single-dose and/or multiple-dose groups.
4. All males in the control group are mated in the first week. If a male should die during or after the first week, no data cards appear for him from that time on; however, there must be at least one data card for him in week one. Control group males are numbered consecutively beginning with 1.
5. Number of each variable should not exceed the following:

<u>Variable</u>	<u>Maximum</u>
Males	20/group
Females	100/week
Weeks in study	8
Females mated to each male	80/8 week period

STATISTICAL PROCEDURE
FOR EVALUATION OF DOMINANT LETHAL DATA

Introduction

In order to determine the mutagenic potential of selected food additives and chemicals, Stanford Research Institute has conducted several dominant lethal tests in mice and rats. Although individual tests differed slightly in details, basic test procedures were to administer compounds orally at different dose levels and frequency to groups of males. These males, as well as control group males for both the single and multiple-dose groups, were mated with two virgin females.

In studies using mice, females were examined daily for the presence of a mating plug (readily detectable in the mouse). When a plug was found, the female was replaced with a new virgin female. Fourteen days after identifying the mating plug, the females were sacrificed, and total implants, early deaths, and late deaths were counted. This continuous breeding and examination procedure was continued for seven weeks.

In studies using rats, females were removed after seven days of cohabitation with the males and replaced with new virgin females. Fourteen to eighteen days after first day of breeding, females were sacrificed and total implants, early deaths, late deaths, and total corpora lutea were counted. This procedure was repeated for eight weeks in the single dose groups and seven weeks in the multiple dose groups.

Autopsy data for each female was coded on work sheets and then punched on computer cards. These data cards, as well as a few cards describing the particulars of the project (duration, number of test groups, number of mated females, etc.), comprise the input to the KLUTE program.

Input

Input to the KLUTE program is a card deck, which was briefly described in the introduction.

Output

Output from KLUTE includes a printed list of the input data and results of several statistical tests.

KLUTE performs the following operations (where each statistical calculation is done once for each week's data):

1. The data cards are read and stored in central memory while a check is made to verify that the number of corpora lutea is greater than or equal to the number of implants. If any data fail this check, the run is aborted and the data are returned for review. The entire set of input data is printed out.
2. The fertility index (the number of pregnant females divided by the number of mated females) is calculated.
3. The chi-square test is done to compare each dosage level to the control on fertility. Let:

N_i = no. of mated females at dose level i,

n_i = no. of pregnant females at dose level i.

Then the chi-square 2 x 2 tables are of the form:

$$\begin{bmatrix} n_0 & n_1 \\ N_0 - n_0 & N_1 - n_1 \end{bmatrix}$$

and chi-squared (with 1 degree of freedom) is:

$$X^2 = \frac{(N_0 + N_1)(|n_0(n_1 - n_1) - n_1(N_0 - n_0)| - (N_0 + N_1)/2)^2}{(n_0 + n_1)(N_0 - n_0 + N_1 - n_1)(N_0)(N_1)} \quad (\text{corrected for continuity})$$

where the subscript 0 represents the control group.*

For each dosage group (including the control group and TEM), the following is printed out: the number of pregnant females (N PRG), the number of mated females (N MTD), the fertility index and X^2 .

4. Armitage's test for a linear trend in proportions is applied to the fertility index. The formula for this calculation is found on pages 246-248 of "Statistical Calculations" by Snedecor and Cochran, 6th Edition, Iowa State University Press, 1967. Using the notation of (3) above, we have a 2 x 3 contingency table of the form:

	<u>dose 1</u>	<u>dose 2</u>	<u>dose 3</u>	<u>row totals</u>
<u>Column Totals</u>	n_1	n_2	n_3	t
	$N_1 - n_1$	$N_2 - n_2$	$N_3 - n_3$	$T-t$
	N_1	N_2	N_3	T

Armitage's "chi-square" is given as $X_{(C-1)}^2 - X_1^2$, where C=3 and

$$X_1^2 = \frac{T(T\Sigma nx - t\Sigma Nx)^2}{t(T-t)(T\Sigma nx^2 - (\Sigma Nx)^2)}, \quad X_{(C-1)}^2 = \frac{T^2(\sum \frac{n^2}{N} - \frac{t^2}{T})}{t(T-t)}$$

*In all tests, the single-dose treatment groups are compared with the single-dose control group and the multiple-dose treatment groups compared with the multiple-dose control group.

where $\sum n_i x_i$ stands for $\sum_{i=1}^3 n_i x_i$, $\sum \frac{n_i^2}{N}$ for $\sum_{i=1}^3 \frac{n_i^2}{N_i}$, etc., and the x_i are the dosage levels.

This calculation is then repeated with x replaced by $\log x$. The Armitage test is also applied to the following 2×4 contingency table:

<u>Control</u>	<u>dose 1</u>	<u>dose 2</u>	<u>dose 3</u>
n_0	n_1	n_2	n_3
$N_0 - n_0$	$N_1 - n_1$	$N_2 - n_2$	$N_3 - n_3$

In this case, $C=4$.

The printout for the Armitage tests includes the degrees of freedom, the number pregnant (N PRG) and the number mated (N MTD) for each of the 3 or 4 groups included in the tests, plus $\chi^2_{(C-1)}$, χ^2_1 and their difference (labeled ARMTG CHISQ).

5. The t-test is applied to determine significant differences between the average number of implantations per pregnant female at a dose level, and the average for the control. Let

n_i = no. of pregnant females at dose level i .

u_{ij} = total no. of implantations for pregnant female j of dose i .

Then,

$$\bar{u}_i = \frac{1}{n_i} \sum_{j=1}^{n_i} u_{ij}$$

$$s_i^2 = \sum_{j=1}^{n_i} (u_{ij} - \bar{u}_i)^2$$

The T-statistic for dose i has $n_o + n_i - 2$ degrees of freedom, and is equal to:

$$t_i = \frac{\bar{u}_o - \bar{u}_i}{\sqrt{\left[\frac{s_o^2 + s_i^2}{n_o + n_i - 2} \left(\frac{1}{n_o} + \frac{1}{n_i} \right) \right]^{1/2}}}$$

The t-test printout gives, for each group: the number pregnant (N PRG), the mean and standard deviation of the number of implantations. The absolute value of T and the degrees of freedom (DF) are given for each treatment group and for TEM.

6. A regression fit of the average number of implantations, \bar{u}_i , is made for both the arithmetic and logarithmic dose (X_i and $\log X_i$) to see which is better.

These two fits include the data from the three treatment groups only. A third regression using the X_i as independent variables includes data from the three treatment groups and the control group.

The regressions are computed as follows:

Let N = the number of observations, i.e., the total number of pregnant females in the groups used in the regression.

X_i = the value of the independent variable (dose or log dose) for the i -th female.

U_i = the value of the dependent variable (number of implantations) for the i -th female.

Then,

$$\bar{X} = \frac{1}{N} \sum_{i=1}^N X_i$$

SD X = standard deviation of the X_i

$$= \left[\frac{1}{N-1} SS_X \right]^{1/2},$$

$$\text{where } SS_X = \sum_{i=1}^N (X_i - \bar{X})^2$$

$$\bar{U} = \frac{1}{N} \sum_{i=1}^N U_i,$$

SD U = standard deviation of the U_i

$$= \left[\frac{1}{N-1} SS_U \right]^{1/2},$$

$$\text{where } SS_U = \sum_{i=1}^N (U_i - \bar{U})^2,$$

$$\text{and } S_{XU} = \sum_{i=1}^N (X_i - \bar{X})(U_i - \bar{U}).$$

From these quantities, we compute:

B = estimate of the slope of the regression line

$$= S_{XU}/SS_X,$$

A = estimate of the intercept of the regression line

$$= \bar{U} - B\bar{X},$$

Also,

$$\begin{aligned} \text{VARU.X} &= \text{variance of } U \text{ about the regression line} \\ &= \frac{\text{SS}_U - (S_{XU})^2 / \text{SS}_X}{N-2} \end{aligned}$$

and from this is computed,

$\text{VARB} = \text{variance of the estimate, B}$

$$= \frac{\text{VARU.X}}{\text{SS}_X}$$

$\text{VARA} = \text{variance of the estimate, A}$

$$= \text{VARU.X} \left[\frac{1}{N} + \frac{\bar{x}^2}{\text{SS}_X} \right]$$

$\text{VARUBAR} = \text{variance of } U,$

$$= \frac{\text{VARU.X}}{N}$$

and

$\text{CV } U.X = \text{coefficient of variation of } U \text{ about } X$

$$= \frac{(\text{VARU.X})^{1/2}}{\bar{U}}$$

And finally we have:

$\text{TB} = \text{the t-statistic for testing the hypothesis that the regression slope is zero}$

$$= \frac{B}{\sqrt{\text{VARB}}}$$

$\text{DF} = \text{number of degrees of freedom for TB}$
 $= N - 2$

7. The preimplantation loss, y_{ij} , is calculated for each pregnant female, j , as the number of corpora lutea, v_{ij} , minus the number of implantations, u_{ij} . Then the Freeman-Tukey transformation is applied to y_{ij} as follows:

$$f_{ij} = \sin^{-1} \sqrt{\frac{y_{ij}}{v_{ij}+1}} + \sin^{-1} \sqrt{\frac{y_{ij}+1}{v_{ij}+1}}$$

The t-test is then applied to the f 's. Let

$$\bar{f}_i = \frac{1}{n_i} \sum_{j=1}^{n_i} f_{ij}$$

$$s_i^2 = \sum_{j=1}^{n_i} (f_{ij} - \bar{f}_i)^2,$$

where n_i , and n_o are defined above (step 3).

Then $t_i = \frac{\bar{f}_o - \bar{f}_i}{\sqrt{\left[\frac{s_o^2 + s_i^2}{n_o + n_i - 2} \left(\frac{1}{n_o} + \frac{1}{n_i} \right) \right]^{1/2}}}$

The printout gives, for each group, the number of pregnant females (N PRG), the mean and standard deviation of the f_{ij} 's. For each treatment group and for TEM, the absolute value of t_i (T), and its degrees of freedom (DF) are given.

8. The number of dead implants, z_{ij} , for each female, j , is the sum of the early and late deaths. The t-test is applied to determine significant differences between the average number of dead implants per pregnant female at a dose level and the average for the control by repeating step 5 above with z_{ij} substituted for u_{ij} .

9. The number of pregnant females with one or more dead implants, m_i , is calculated. In the printout, the m_i are referred to as N WDI (i.e., "number with dead implants").

10. The chi-square test and Armitage's test for a linear trend is calculated for the proportion of pregnant females with one or more dead implants,

$$p_i = \frac{m_i}{n_i}$$

by repeating steps 3 and 4, above, with m_i substituted for n_i , and n_i substituted for N_i .

In the printout, the ratio, p_i , is called the "death index", in analogy with the fertility index.

11. The ratios, p_i , computed above, undergo a probit analysis to determine whether the probit of this proportion is linearly related to the log dose. Computer subroutine PROBT, from the IBM System/360 Scientific Subroutine Package Version III, is used to compute A and B and the χ^2 statistic for the regression equation,

$$P_i = A + B * \log x_i$$

where P_i is derived by the program from

$$\int_{-\infty}^{P_i - 5} N_x(0,1)dx = p_i.$$

$(N_x(0,1))$ is the normal curve, with a mean of 0 and a standard deviation of 1).

12. The number of dead implants, z_{ij} , and the number of total implants, u_{ij} , are calculated for each pregnant female, j. The Freeman-Tukey transformation and subsequent t-test is applied to this data by repeating step 7, above, as follows:

$$f_{ij} = \sin^{-1} \sqrt{\frac{z_{ij}}{u_{ij}+1}} + \sin^{-1} \sqrt{\frac{z_{ij+1}}{u_{ij+1}+1}}$$

$$\bar{f}_i = \frac{1}{n_i} \sum_{j=1}^{n_i} f_{ij}$$

$$s_i^2 = \sum_{j=1}^{n_i} (f_{ij} - \bar{f}_i)^2$$

$$t_i = \frac{\bar{f}_o - \bar{f}_i}{\left[\frac{s_o^2 + s_i^2}{n_o + n_i - 2} \left(\frac{1}{n_o} + \frac{1}{n_i} \right) \right]^{1/2}}$$

13. Five one-way analyses of variance are performed on the control groups' data. The five variables analyzed are:

- a. Number of pregnant females,
- b. Number of implantations per pregnant female,
- c. The pre-implantation loss (as defined in Step 7) per pregnant female,
- d. The number of dead implants per pregnant female,
- e. The ratio of dead implants to the total implants per pregnant female.

In view of the fact that none of the variables on which the one-way analysis of variance have been performed is even approximately normal in distribution, the probability levels associated with these analyses of variances are necessarily approximate.

For case a., R_{kj} equals 1 if female j assigned to male k became pregnant; otherwise R_{kj} equals zero. For cases b. through e. the tabulation is limited to data for pregnant females; i.e., R_{kj} equals the value of the specified variable for female j assigned to male k if the female was pregnant; data for non-pregnant females are excluded.

For case a., L_k equals the number of females assigned to male k. For cases b. through e., L_k equals the number of females assigned to male k that became pregnant.

For each of these variables the ANOVA calculations are as follows:

M is the number of males

$$\bar{R}_k = \frac{1}{L_k} \sum_{j=1}^{L_k} R_{kj}$$

$$\bar{R} = \frac{1}{M} \sum_{k=1}^M \bar{R}_k$$

Then, the sum-of-squares-within-males = $SUMSQ_w$

$$= \sum_{k=1}^M = \sum_{j=1}^{L_k} (R_{kj} - \bar{R}_k)^2,$$

the degrees-of-freedom-within-males = DF_w

$$= \sum_{k=1}^M (L_k - 1),$$

and the mean-square-within-males = $MEANSQ_w = \frac{SUMSQ_w}{DF_w}$.

Similarly, the sum-of-squares-between-males = $SUMSQ_B = \sum_{k=1}^M L_k (\bar{R}_k - \bar{R})^2$,

the degrees-of-freedom-between-males = $DF_B = M-1$,

and the mean-square-between-males = $MEANSQ_B = \frac{SUMSQ_B}{DF_B}$.

Finally, the F-ratio is $F = \frac{MEANSQ_B}{MEANSQ_w}$.

In the printout, these quantities are labeled without the subscripts, but the "within" and "between" quantities are identified by the page heading.

Also, the total-sum-of-squares = $SUMSQ_w + SUMSQ_B$.

and its degrees-of-freedom

$$= \sum_{k=1}^M L_k - 1,$$

printed.

14. The t-test is applied to determine significant differences between the average number of corpora lutea per pregnant female at a dose level, and the average for the control. Let

$$n_i = \text{no. of pregnant females at dose level } i.$$

$$c_{ij} = \text{total no. of corpora lutea for pregnant female } j \text{ of dose } i.$$

Then,

$$\bar{c}_i = \frac{1}{n_i} \sum_{j=1}^{n_i} c_{ij}$$

$$s_i^2 = \sum_{j=1}^{n_i} (c_{ij} - \bar{c}_i)^2$$

The T-statistic for dose i has $n_o + n_i - 2$ degrees of freedom, and is equal to:

$$t_i = \frac{\bar{c}_o - \bar{c}_i}{\sqrt{\left[\frac{s_o^2 + s_i^2}{n_o + n_i - 2} \left(\frac{1}{n_o} + \frac{1}{n_i} \right) \right]}}^{1/2}$$

The t-test printout gives, for each group: the number pregnant (N PRG), the mean and standard deviation of the number of corpora lutea. The absolute value of T and the degrees of freedom (DF) are given for each treatment group and for TEM.

APPENDIX B

RAW DATA AND STATISTICAL ANALYSES

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DOMINANT LETHAL STUDY OF COMPOUND 71-71

MANGANESE SULFATE

PAGE 1

TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CUMPURA LUTEA	
							L	H	L	H	L	H
CONTROL	1	S 0.00000	1	1	Y	5	7	0	0	0	0	5
CONTROL	1	S 0.00000	1	2	N	0	0	0	0	0	0	0
CONTROL	1	S 0.00000	2	3	N	0	0	0	0	0	0	0
CONTROL	1	S 0.00000	2	4	Y	6	9	0	0	0	0	6
CONTROL	1	S 0.00000	3	5	Y	6	8	0	0	0	0	6
CONTROL	1	S 0.00000	3	6	Y	5	6	0	0	0	0	5
CONTROL	1	S 0.00000	4	7	N	0	0	1	0	1	1	9
CONTROL	1	S 0.00000	4	8	Y	4	6	0	0	0	1	5
CONTROL	1	S 0.00000	5	9	Y	4	8	0	0	0	0	8
CONTROL	1	S 0.00000	6	10	N	0	0	0	0	0	0	7
CONTROL	1	S 0.00000	6	11	Y	7	7	0	0	0	0	7
CONTROL	1	S 0.00000	6	12	Y	8	4	0	0	0	0	8
CONTROL	1	S 0.00000	7	13	Y	4	5	0	0	0	0	5
CONTROL	1	S 0.00000	7	14	Y	5	6	0	0	0	0	6
CONTROL	1	S 0.00000	8	15	Y	5	5	0	0	0	0	5
CONTROL	1	S 0.00000	8	16	Y	0	1	0	0	0	0	9
CONTROL	1	S 0.00000	9	17	Y	7	6	0	0	1	0	7
CONTROL	1	S 0.00000	9	18	Y	7	8	0	0	0	0	8
CONTROL	1	S 0.00000	10	19	N	0	0	0	0	0	0	0
CONTROL	1	S 0.00000	10	20	Y	6	7	0	0	1	0	6
71-71	1	S .01200	81	161	Y	2	0	0	0	0	0	7
71-71	1	S .01200	81	162	Y	5	6	0	0	0	0	5
71-71	1	S .01200	82	163	Y	8	5	0	0	0	0	8
71-71	1	S .01200	82	164	Y	7	6	0	1	0	0	6
71-71	1	S .01200	83	165	Y	6	5	0	0	0	0	6
71-71	1	S .01200	83	166	Y	6	6	0	0	0	0	6
71-71	1	S .01200	84	167	Y	9	6	0	0	1	0	9
71-71	1	S .01200	84	168	Y	7	5	0	0	1	0	6
71-71	1	S .01200	85	169	Y	9	0	0	0	0	0	9
71-71	1	S .01200	85	170	Y	11	3	0	0	0	0	11
71-71	1	S .01200	86	171	Y	7	5	1	0	0	0	8
71-71	1	S .01200	86	172	Y	10	5	0	0	0	0	10
71-71	1	S .01200	87	173	Y	6	6	0	0	1	0	7
71-71	1	S .01200	87	174	Y	5	9	0	1	0	0	5
71-71	1	S .01200	88	175	Y	6	5	1	0	0	0	6
71-71	1	S .01200	88	176	Y	6	6	0	0	0	0	6
71-71	1	S .01200	89	177	Y	5	7	0	0	0	0	8
71-71	1	S .01200	89	178	Y	7	4	0	0	0	0	6
71-71	1	S .01200	90	179	Y	3	7	0	0	0	0	3
71-71	1	S .01200	90	180	Y	5	6	0	0	0	0	5

DOMINANT LETHAL STUDY OF COMPOUND 71-71

MANGANESE SULFATE

PAGE 2

TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PRFG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	R	L	R	L	R
71-71	1	S	.12000	91	181	Y	6	7	0	0	0	0	6	7
71-71	1	S	.12000	91	182	Y	4	6	0	2	0	1	8	10
71-71	1	S	.12000	92	183	Y	2	4	0	0	0	0	4	9
71-71	1	S	.12000	92	184	Y	5	8	0	0	0	2	5	5
71-71	1	S	.12000	93	185	Y	5	5	1	0	0	0	8	4
71-71	1	S	.12000	93	186	Y	5	8	0	0	1	1	5	9
71-71	1	S	.12000	94	187	Y	6	6	0	0	0	0	7	6
71-71	1	S	.12000	94	188	Y	4	4	0	0	0	0	4	H
71-71	1	S	.12000	95	189	N	0	0	0	0	0	0	0	0
71-71	1	S	.12000	95	190	Y	7	7	0	0	0	0	7	7
71-71	1	S	.12000	96	191	Y	0	0	0	0	0	0	0	0
71-71	1	S	.12000	96	192	N	3	10	1	1	0	0	4	11
71-71	1	S	.12000	97	193	Y	9	3	0	0	0	0	9	4
71-71	1	S	.12000	97	194	N	0	0	0	0	0	0	0	0
71-71	1	S	.12000	98	195	Y	5	6	0	0	0	0	5	6
71-71	1	S	.12000	98	196	Y	1	0	1	0	0	0	9	10
71-71	1	S	.12000	99	197	N	0	0	0	0	0	0	0	0
71-71	1	S	.12000	99	198	Y	5	8	0	0	1	2	5	9
71-71	1	S	.12000	100	199	Y	5	5	0	0	0	1	6	5
71-71	1	S	.12000	100	200	Y	6	5	0	0	0	0	0	0
71-71	1	S	1.20000	101	201	Y	5	8	0	0	0	0	5	8
71-71	1	S	1.20000	101	202	Y	7	5	0	0	0	0	7	5
71-71	1	S	1.20000	102	203	Y	6	7	0	0	0	0	6	7
71-71	1	S	1.20000	102	204	Y	7	4	0	0	0	0	7	4
71-71	1	S	1.20000	103	205	Y	3	7	0	0	0	0	5	9
71-71	1	S	1.20000	103	206	Y	9	3	0	0	0	0	11	4
71-71	1	S	1.20000	104	207	Y	3	10	0	0	0	1	4	10
71-71	1	S	1.20000	104	208	Y	4	7	0	0	0	0	4	7
71-71	1	S	1.20000	105	209	Y	4	7	0	0	0	0	4	7
71-71	1	S	1.20000	105	210	Y	8	3	0	0	0	0	8	3
71-71	1	S	1.20000	106	211	Y	5	3	0	0	0	0	5	6
71-71	1	S	1.20000	106	212	Y	7	5	1	0	0	0	8	7
71-71	1	S	1.20000	107	213	Y	7	6	0	0	0	0	7	6
71-71	1	S	1.20000	107	214	Y	5	7	0	0	0	0	5	8
71-71	1	S	1.20000	108	215	Y	6	8	0	0	0	0	6	8
71-71	1	S	1.20000	108	216	Y	3	9	0	0	2	0	3	10
71-71	1	S	1.20000	109	217	Y	8	6	0	0	2	0	0	0
71-71	1	S	1.20000	109	218	N	0	0	0	0	0	0	7	7
71-71	1	S	1.20000	110	219	Y	6	6	7	0	0	0	7	6
71-71	1	S	1.20000	110	220	Y	6	6	0	0	0	0	6	6

DOMINANT LETHAL STUDY OF COMPOUND 71-71

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DOMINANT LETHAL STUDY OF COMPOUND 71-71

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PRFG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		COMPOUND LUTEA	
							L	R	L	R	L	R	L	R
71-71	1	M	.01200	71	141	Y	5	6	0	0	0	0	6	6
71-71	1	M	.01200	71	142	Y	7	6	0	0	1	0	7	6
71-71	1	M	.01200	72	143	Y	4	6	0	0	0	0	5	7
71-71	1	M	.01200	72	144	Y	6	5	1	0	0	0	6	5
71-71	1	M	.01200	73	145	Y	3	10	0	0	0	2	5	10
71-71	1	M	.01200	73	146	Y	6	5	0	0	0	0	6	7
71-71	1	M	.01200	74	147	Y	4	8	0	0	1	0	4	7
71-71	1	M	.01200	74	148	Y	4	7	0	0	1	0	7	6
71-71	1	M	.01200	75	149	Y	7	6	0	0	0	0	0	0
71-71	1	M	.01200	75	150	N	0	6	0	0	0	0	4	6
71-71	1	M	.01200	76	151	Y	4	5	0	0	0	0	7	6
71-71	1	M	.01200	76	152	Y	7	6	0	0	0	0	5	8
71-71	1	M	.01200	77	153	Y	0	1	0	0	0	0	7	5
71-71	1	M	.01200	77	154	Y	7	5	0	0	0	0	0	0
71-71	1	M	.01200	78	155	N	0	3	0	0	0	0	8	4
71-71	1	M	.01200	78	156	Y	7	3	0	0	0	0	7	13
71-71	1	M	.01200	79	157	Y	4	9	0	0	0	4	1	7
71-71	1	M	.01200	79	158	Y	6	4	0	0	0	1	7	6
71-71	1	M	.01200	80	159	Y	7	5	0	0	0	0	7	5
71-71	1	M	.01200	80	160	Y	4	10	0	0	0	2	4	10
71-71	1	M	.12000	81	161	Y	4	6	0	0	0	0	5	7
71-71	1	M	.12000	81	162	Y	7	6	1	0	0	0	7	6
71-71	1	M	.12000	82	163	Y	4	9	0	0	0	0	4	6
71-71	1	M	.12000	82	164	Y	4	6	0	0	0	0	4	8
71-71	1	M	.12000	83	165	Y	5	6	0	0	0	0	5	9
71-71	1	M	.12000	83	166	Y	8	4	1	1	0	0	0	0
71-71	1	M	.12000	84	167	N	0	0	0	0	0	0	0	0
71-71	1	M	.12000	84	168	N	8	5	0	0	1	2	1	8
71-71	1	M	.12000	85	169	Y	7	5	0	0	0	1	7	5
71-71	1	M	.12000	85	170	Y	0	0	0	0	0	0	0	0
71-71	1	M	.12000	86	171	N	0	0	0	0	0	0	0	0
71-71	1	M	.12000	86	172	N	0	0	0	0	0	0	5	0
71-71	1	M	.12000	87	173	Y	5	8	0	1	0	0	7	8
71-71	1	M	.12000	87	174	Y	7	7	0	0	0	0	8	7
71-71	1	M	.12000	88	175	Y	6	7	0	0	0	0	6	5
71-71	1	M	.12000	88	176	Y	0	1	0	0	0	1	3	7
71-71	1	M	.12000	89	177	Y	3	7	0	1	1	0	0	0
71-71	1	M	.12000	89	178	Y	7	6	1	0	0	0	7	6
71-71	1	M	.12000	90	179	Y	3	6	0	0	0	0	3	4
71-71	1	M	.12000	90	180	Y	5	4	0	0	0	0	8	4

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DOMINANT LETHAL STUDY OF COMPOUND 71-71

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PRFG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	R	L	R
CONTROL	2	S 0.00000	1	1	Y	5	6	0	1	0	0	5
CONTROL	2	S 0.00000	1	2	YY	5	7	0	0	0	0	5
CONTROL	2	S 0.00000	2	3	Y	1	6	0	0	0	0	6
CONTROL	2	S 0.00000	2	4	Y	3	6	0	0	0	0	3
CONTROL	2	S 0.00000	3	5	YY	6	6	0	0	0	0	6
CONTROL	2	S 0.00000	3	6	YY	5	5	0	0	0	0	5
CONTROL	2	S 0.00000	4	7	YY	6	7	0	0	0	0	6
CONTROL	2	S 0.00000	4	8	YY	5	7	0	0	0	0	5
CONTROL	2	S 0.00000	5	9	YY	2	5	0	0	1	1	5
CONTROL	2	S 0.00000	5	10	YY	4	8	0	0	1	1	5
CONTROL	2	S 0.00000	6	11	YY	4	6	0	0	0	0	4
CONTROL	2	S 0.00000	6	12	YY	4	5	0	0	0	0	4
CONTROL	2	S 0.00000	7	13	YY	6	8	0	0	0	0	7
CONTROL	2	S 0.00000	7	14	YY	7	6	0	0	0	0	7
CONTROL	2	S 0.00000	8	15	YY	1	9	0	0	0	0	2
CONTROL	2	S 0.00000	8	16	YY	6	6	0	0	0	0	6
CONTROL	2	S 0.00000	9	17	YY	5	7	0	0	0	0	7
CONTROL	2	S 0.00000	9	18	YY	5	7	1	0	0	0	5
CONTROL	2	S 0.00000	10	19	YY	7	6	0	0	0	0	7
CONTROL	2	S 0.00000	10	20	Y	2	5	0	0	0	0	3
71-71	2	S .01200	81	161	Y	6	5	0	2	0	0	6
71-71	2	S .01200	81	162	YY	2	7	0	0	0	0	2
71-71	2	S .01200	82	163	YY	5	7	0	1	0	0	5
71-71	2	S .01200	82	164	YY	5	7	0	1	0	0	5
71-71	2	S .01200	83	165	YY	8	5	0	0	0	0	8
71-71	2	S .01200	83	166	YY	6	4	0	0	0	0	8
71-71	2	S .01200	84	167	YY	8	2	1	0	0	0	2
71-71	2	S .01200	84	168	YY	6	3	0	0	0	0	7
71-71	2	S .01200	85	169	YY	7	5	0	0	0	0	7
71-71	2	S .01200	85	170	YY	7	6	0	0	0	0	6
71-71	2	S .01200	86	171	YY	6	5	0	0	0	0	5
71-71	2	S .01200	86	172	YY	5	7	0	0	0	0	8
71-71	2	S .01200	87	173	YY	7	6	0	0	0	0	7
71-71	2	S .01200	87	174	YY	3	7	1	0	0	0	4
71-71	2	S .01200	88	175	YY	4	8	0	0	0	0	8
71-71	2	S .01200	88	176	YY	7	3	0	0	0	0	7
71-71	2	S .01200	89	177	YY	5	4	0	0	1	0	5
71-71	2	S .01200	89	178	YY	6	6	0	1	1	0	6
71-71	2	S .01200	90	179	YY	0	0	0	0	0	0	7
71-71	2	S .01200	90	180	N	0	0	0	0	0	0	0

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		COPHORA LUTEA	
							L	R	L	H	L	H	L	R
71-71	2	S	.12000	91	181	Y	4	5	0	0	0	0	6	5
71-71	2	S	.12000	91	182	YY	5	5	0	0	0	0	5	6
71-71	2	S	.12000	92	183	YY	5	3	0	0	0	0	5	3
71-71	2	S	.12000	92	184	N	0	0	0	0	0	0	0	0
71-71	2	S	.12000	93	185	Y	8	5	0	0	0	0	8	6
71-71	2	S	.12000	93	186	N	0	0	0	0	0	0	0	0
71-71	2	S	.12000	94	187	YY	5	7	0	0	0	0	5	7
71-71	2	S	.12000	94	188	YY	3	9	1	1	0	0	3	10
71-71	2	S	.12000	95	189	YY	3	4	0	0	0	0	3	8
71-71	2	S	.12000	95	190	YY	6	5	0	0	0	0	6	5
71-71	2	S	.12000	96	191	YY	6	4	0	1	0	0	7	5
71-71	2	S	.12000	96	192	YY	8	5	0	0	0	0	8	5
71-71	2	S	.12000	97	193	YY	7	3	1	0	0	0	10	5
71-71	2	S	.12000	97	194	YY	4	12	1	0	0	0	4	12
71-71	2	S	.12000	98	195	YY	5	6	1	0	0	0	5	6
71-71	2	S	.12000	98	196	NY	0	0	0	0	0	0	0	0
71-71	2	S	.12000	99	197	YY	3	9	0	0	1	0	4	9
71-71	2	S	.12000	99	198	N	0	0	0	0	0	0	0	0
71-71	2	S	.12000	100	199	YY	4	8	0	0	0	0	4	9
71-71	2	S	.12000	100	200	Y	3	6	0	1	0	2	5	6
71-71	2	S	1.20000	101	201	Y	5	6	0	0	0	0	5	7
71-71	2	S	1.20000	101	202	YY	4	5	0	0	0	0	4	6
71-71	2	S	1.20000	102	203	YY	10	2	0	0	0	1	10	2
71-71	2	S	1.20000	102	204	YY	4	11	0	0	0	0	4	11
71-71	2	S	1.20000	103	205	YY	7	6	1	0	0	0	8	6
71-71	2	S	1.20000	103	206	YY	4	7	0	0	0	0	4	7
71-71	2	S	1.20000	104	207	YY	7	6	0	0	0	0	7	6
71-71	2	S	1.20000	104	208	YY	7	5	0	0	0	0	7	5
71-71	2	S	1.20000	105	209	YY	4	8	0	0	0	0	4	8
71-71	2	S	1.20000	105	210	YY	4	4	0	0	0	0	5	4
71-71	2	S	1.20000	106	211	Y	6	4	1	0	0	0	6	5
71-71	2	S	1.20000	106	212	YY	2	8	0	2	0	1	2	9
71-71	2	S	1.20000	107	213	YY	6	5	0	0	1	0	7	6
71-71	2	S	1.20000	107	214	YY	4	7	0	1	0	0	4	7
71-71	2	S	1.20000	108	215	YY	6	8	0	0	1	0	6	8
71-71	2	S	1.20000	108	216	YY	6	9	0	1	0	0	6	10
71-71	2	S	1.20000	109	217	YY	8	3	0	0	0	0	8	4
71-71	2	S	1.20000	109	218	YY	11	1	0	0	1	0	11	3
71-71	2	S	1.20000	110	219	YY	8	5	0	0	0	0	8	6
71-71	2	S	1.20000	110	220	Y	6	3	2	0	0	1	6	4

DOMINANT LETHAL STUDY OF COMPOUND 71-71

~~CANESE SULFATE~~

PAGE **K**

TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PKFG.	IMPLANTS L R	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA L R	
								L	R	L	R	L	R
TEM	2	S	.00020	11	21	Y	4 7	0 5	0 4	0 1	0 0	2 0	4 9
TEM	2	S	.00020	11	22	Y	7 4	2 4	3 1	1 0	0 0	0 0	7 4
TEM	2	S	.00020	12	23	Y	5 6	0 5	0 4	0 0	0 0	0 0	8 6
TEM	2	S	.00020	12	24	Y	6 4	0 4	0 4	0 0	0 0	0 0	7 5
TEM	2	S	.00020	13	25	Y	4 4	0 4	0 1	0 0	0 0	0 0	7 6
TEM	2	S	.00020	13	26	Y	4 4	0 4	0 1	0 0	0 0	0 0	2 10
TEM	2	S	.00020	14	27	Y	1 1	1 1	1 1	1 2	0 0	0 0	4 7
TEM	2	S	.00020	14	28	Y	4 4	5 5	3 4	6 6	0 0	0 0	6 6
TEM	2	S	.00020	15	29	Y	4 4	7 5	4 4	3 3	0 0	0 0	4 10
TEM	2	S	.00020	15	30	Y	5 5	5 5	4 4	3 3	0 0	0 0	6 5
TEM	2	S	.00020	16	31	Y	4 4	8 5	5 5	4 4	3 3	0 0	7 3
TEM	2	S	.00020	16	32	Y	4 4	8 5	5 5	4 4	3 3	0 0	5 5
TEM	2	S	.00020	17	33	Y	5 5	6 6	4 4	4 4	3 3	0 0	12 10
TEM	2	S	.00020	17	34	Y	5 5	6 6	4 4	4 4	3 3	0 0	7 7
TEM	2	S	.00020	18	35	Y	6 6	4 4	0 0	0 0	0 0	0 0	6 6
TEM	2	S	.00020	18	36	Y	6 6	4 4	0 0	0 0	0 0	0 0	8 8
TEM	2	S	.00020	19	37	Y	8 8	2 2	7 7	6 6	0 0	0 0	8 8
TEM	2	S	.00020	19	38	Y	8 8	2 2	7 7	6 6	0 0	0 0	7 7
TEM	2	S	.00020	20	39	Y	7 7	5 5	7 7	7 7	0 0	0 0	2 3
TEM	2	S	.00020	20	40	Y	2 2	6 6	2 2	4 4	0 0	0 0	0 0
CONTROL	2	M	0.00000	1	1	Y	3 10	5 8	0 0	1 0	0 0	0 0	3 10
CONTROL	2	M	0.00000	1	2	Y	7 6	7 6	0 0	0 0	0 0	0 0	7 7
CONTROL	2	M	0.00000	2	3	Y	4 7	4 7	0 0	0 0	0 0	0 0	4 7
CONTROL	2	M	0.00000	2	4	Y	4 7	7 7	0 0	0 0	0 0	0 0	5 5
CONTROL	2	M	0.00000	3	5	Y	6 5	5 5	1 1	0 0	0 0	0 0	10 10
CONTROL	2	M	0.00000	3	6	Y	9 3	3 3	0 0	0 0	0 0	0 0	6 6
CONTROL	2	M	0.00000	4	7	Y	6 7	7 7	1 1	0 0	0 0	0 0	5 5
CONTROL	2	M	0.00000	4	8	Y	5 7	7 7	0 0	0 0	0 0	0 0	8 8
CONTROL	2	M	0.00000	5	9	Y	8 7	7 7	0 0	0 0	0 0	0 0	8 8
CONTROL	2	M	0.00000	5	10	Y	8 8	8 8	0 0	0 0	0 0	0 0	8 8
CONTROL	2	M	0.00000	6	11	Y	4 8	8 8	0 0	0 0	0 0	0 0	4 4
CONTROL	2	M	0.00000	6	12	Y	4 8	8 8	0 0	0 0	0 0	0 0	4 4
CONTROL	2	M	0.00000	7	13	Y	8 6	6 6	2 2	1 1	0 0	0 0	8 8
CONTROL	2	M	0.00000	7	14	Y	7 6	7 6	0 0	0 0	0 0	0 0	7 7
CONTROL	2	M	0.00000	8	15	Y	6 6	6 6	0 0	0 0	0 0	0 0	6 6
CONTROL	2	M	0.00000	8	16	Y	8 5	5 5	1 1	0 0	0 0	0 0	9 9
CONTROL	2	M	0.00000	9	17	Y	5 5	3 3	1 1	0 0	0 0	0 0	6 6
CONTROL	2	M	0.00000	9	18	Y	5 5	3 3	1 1	0 0	0 0	0 0	5 5
CONTROL	2	M	0.00000	10	19	Y	5 5	7 12	0 0	0 0	0 0	0 0	7 7
CONTROL	2	M	0.00000	10	20	Y	1 12	0 0	0 0	0 0	0 0	0 0	2 12

DOMINANT LETHAL STUDY OF COMPOUND 71-71

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA		
								L	R	L	R	L	R	
71-71	2	M	.01200	71	141	Y	7	6	0	0	0	0	7	8
71-71	2	M	.01200	71	142	Y	0	8	0	0	0	0	5	6
71-71	2	M	.01200	72	143	Y	5	5	0	0	0	0	6	6
71-71	2	M	.01200	72	144	Y	6	6	1	0	1	0	6	6
71-71	2	M	.01200	73	145	Y	6	7	3	2	0	0	6	6
71-71	2	M	.01200	73	146	Y	6	9	1	0	0	0	9	8
71-71	2	M	.01200	74	147	Y	4	8	0	0	0	0	4	4
71-71	2	M	.01200	74	148	Y	4	6	0	0	0	0	6	6
71-71	2	M	.01200	76	151	Y	4	7	0	0	0	0	4	4
71-71	2	M	.01200	76	152	Y	0	0	0	0	0	0	0	0
71-71	2	M	.01200	77	153	N	3	11	0	1	1	4	3	4
71-71	2	M	.01200	77	154	Y	4	5	0	0	0	0	7	8
71-71	2	M	.01200	78	155	Y	6	7	1	2	0	0	6	8
71-71	2	M	.01200	78	156	Y	6	7	0	1	2	0	5	8
71-71	2	M	.01200	79	157	Y	6	8	5	0	0	0	8	5
71-71	2	M	.01200	79	158	Y	7	4	0	0	0	0	7	5
71-71	2	M	.01200	80	159	Y	6	4	1	0	0	0	6	6
71-71	2	M	.01200	80	160	Y	0	0	0	0	0	0	0	0
71-71	2	M	.12000	81	161	Y	3	11	0	0	0	0	3	11
71-71	2	M	.12000	81	162	Y	4	10	0	0	0	0	7	11
71-71	2	M	.12000	82	163	Y	5	8	0	0	0	0	5	8
71-71	2	M	.12000	82	164	Y	8	6	0	0	0	0	7	7
71-71	2	M	.12000	83	165	Y	6	7	0	0	0	0	6	9
71-71	2	M	.12000	83	166	Y	9	4	1	0	0	0	9	4
71-71	2	M	.12000	83	167	Y	0	8	0	1	1	0	5	5
71-71	2	M	.12000	84	168	Y	5	6	0	0	0	0	7	8
71-71	2	M	.12000	85	169	Y	7	6	0	2	0	0	3	6
71-71	2	M	.12000	85	170	Y	3	5	0	0	0	0	5	10
71-71	2	M	.12000	86	171	Y	5	8	0	2	0	0	5	8
71-71	2	M	.12000	86	172	Y	5	6	0	0	0	0	4	10
71-71	2	M	.12000	87	173	Y	8	4	0	0	0	0	5	10
71-71	2	M	.12000	87	174	Y	4	6	1	0	0	0	6	6
71-71	2	M	.12000	88	175	Y	3	5	0	0	0	0	3	9
71-71	2	M	.12000	88	176	Y	7	6	1	0	0	0	6	7
71-71	2	M	.12000	89	177	Y	2	9	0	0	0	0	9	9
71-71	2	M	.12000	89	178	N	0	8	0	0	0	0	0	0
71-71	2	M	.12000	90	179	Y	5	8	0	0	0	0	0	0
71-71	2	M	.12000	90	180	Y	0	8	1	0	0	0	0	0

DOMINANT LETHAL STUDY OF COMPOUND 71-71

MANGANESE SULFATE

PAGE 10

TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PRFG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	R	L	R	L	R
71-71	2	M 1.20000	91	181		Y	3	9	0	0	0	0	3	9
71-71	2	M 1.20000	91	182		Y	6	5	1	0	0	0	5	5
71-71	2	M 1.20000	92	183		Y	7	3	0	1	0	0	8	5
71-71	2	M 1.20000	92	184		Y	6	6	0	0	0	0	6	7
71-71	2	M 1.20000	93	185		Y	6	6	0	0	0	0	6	6
71-71	2	M 1.20000	93	186		Y	5	7	0	0	0	0	7	8
71-71	2	M 1.20000	94	187		Y	8	5	1	0	0	0	8	5
71-71	2	M 1.20000	94	188		Y	6	7	3	1	0	0	6	7
71-71	2	M 1.20000	95	189		Y	6	5	0	0	0	0	7	5
71-71	2	M 1.20000	95	190		Y	7	7	0	0	0	0	7	8
71-71	2	M 1.20000	96	191		Y	9	7	0	0	0	0	9	7
71-71	2	M 1.20000	96	192		Y	8	5	0	0	0	0	8	7
71-71	2	M 1.20000	97	193		Y	8	6	1	0	0	0	7	8
71-71	2	M 1.20000	97	194		Y	6	8	0	0	0	0	10	7
71-71	2	M 1.20000	98	195		Y	10	6	4	1	0	0	7	9
71-71	2	M 1.20000	98	196		Y	6	8	1	1	1	2	9	5
71-71	2	M 1.20000	99	197		Y	9	5	0	0	0	0	8	7
71-71	2	M 1.20000	99	198		Y	6	7	0	0	0	0	5	8
71-71	2	M 1.20000	100	199		Y	5	8	0	0	0	0	1	8
71-71	2	M 1.20000	100	200		Y	7	5	0	1	0	0	7	7

DOMINANT LETHAL STUDY OF COMPOUND 71-71

MAGNETESE SULFATE

PAGE 11

TEST MATERIAL	WEEK	S/M DOSE NO.	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
						L	H	L	H	L	H	L	H
CONTROL	3	S 0.00000	1	1	Y	7	5	1	0	0	0	8	5
CONTROL	3	S 0.00000	1	2	Y	3	7	0	2	0	0	4	9
CONTROL	3	S 0.00000	2	3	Y	4	10	0	0	0	0	4	10
CONTROL	3	S 0.00000	2	4	Y	3	10	0	0	0	0	5	9
CONTROL	3	S 0.00000	3	5	Y	5	7	0	0	0	0	11	3
CONTROL	3	S 0.00000	3	6	Y	11	3	0	0	0	0	7	4
CONTROL	3	S 0.00000	4	7	Y	7	3	0	0	0	0	8	6
CONTROL	3	S 0.00000	4	8	Y	8	5	0	0	0	0	5	7
CONTROL	3	S 0.00000	5	9	Y	5	7	0	0	0	0	8	3
CONTROL	3	S 0.00000	5	10	Y	8	2	0	0	1	1	9	6
CONTROL	3	S 0.00000	6	11	Y	9	5	0	0	0	0	5	7
CONTROL	3	S 0.00000	6	12	Y	5	7	0	0	0	0	5	5
CONTROL	3	S 0.00000	7	13	Y	5	5	0	0	0	0	7	4
CONTROL	3	S 0.00000	7	14	Y	5	5	0	0	0	0	7	6
CONTROL	3	S 0.00000	8	15	Y	7	4	4	2	0	0	8	6
CONTROL	3	S 0.00000	8	16	Y	7	6	0	0	0	0	6	4
CONTROL	3	S 0.00000	9	17	Y	6	4	0	0	1	0	9	4
CONTROL	3	S 0.00000	9	18	Y	6	4	0	0	0	0	7	4
CONTROL	3	S 0.00000	10	19	Y	9	9	0	0	0	2	7	7
CONTROL	3	S 0.00000	10	20	Y	7	9	0	0	0	0	3	8
71-71	3	S .01200	81	161	Y	3	H	0	0	1	0	4	5
71-71	3	S .01200	81	162	Y	3	5	0	0	0	0	7	5
71-71	3	S .01200	82	163	Y	7	5	0	1	0	0	3	10
71-71	3	S .01200	82	164	Y	3	10	0	1	1	0	9	4
71-71	3	S .01200	83	165	Y	8	4	1	0	1	0	6	7
71-71	3	S .01200	83	166	Y	6	7	0	0	0	0	6	6
71-71	3	S .01200	84	167	Y	6	7	0	0	1	0	6	6
71-71	3	S .01200	84	168	Y	6	6	1	0	0	0	6	6
71-71	3	S .01200	85	169	Y	6	5	1	0	0	0	6	7
71-71	3	S .01200	85	170	Y	6	7	0	0	0	0	10	6
71-71	3	S .01200	86	171	Y	8	4	0	0	0	0	5	9
71-71	3	S .01200	86	172	Y	5	9	0	0	0	0	7	7
71-71	3	S .01200	87	173	Y	7	7	0	1	2	0	10	4
71-71	3	S .01200	87	174	Y	7	4	1	0	0	0	3	10
71-71	3	S .01200	88	175	Y	3	10	0	0	0	0	7	4
71-71	3	S .01200	88	176	Y	7	7	1	0	0	0	11	8
71-71	3	S .01200	89	177	Y	5	5	0	2	0	0	5	4
71-71	3	S .01200	89	178	Y	10	4	0	0	0	0	11	6
71-71	3	S .01200	90	179	Y	7	6	0	0	0	0	8	6
71-71	3	S .01200	90	180	Y	5	6	0	0	0	0	11	8

DOMINANT LETHAL STUDY OF COMPOUND 71-71

MANGANESE SULFATE

PAGE 12

TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PRFG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	R	L	R	L	R
71-71	3	S	.12000	91	181	Y	3	8	0	1	0	0	6	8
71-71	3	S	.12000	91	182	Y	6	3	0	0	0	0	6	3
71-71	3	S	.12000	92	183	Y	7	5	0	0	0	0	7	5
71-71	3	S	.12000	92	184	Y	5	6	0	2	0	0	6	7
71-71	3	S	.12000	93	185	Y	6	5	0	0	0	0	6	5
71-71	3	S	.12000	93	186	N	0	0	0	0	0	0	0	0
71-71	3	S	.12000	94	187	Y	2	3	2	3	0	0	6	8
71-71	3	S	.12000	94	188	Y	8	6	0	0	0	0	9	6
71-71	3	S	.12000	95	189	Y	4	7	0	1	0	0	4	8
71-71	3	S	.12000	95	190	Y	4	9	0	1	0	0	4	9
71-71	3	S	.12000	96	191	Y	6	5	0	1	0	0	6	6
71-71	3	S	.12000	96	192	Y	5	5	0	1	0	0	5	7
71-71	3	S	.12000	97	193	N	0	0	0	0	0	0	0	0
71-71	3	S	.12000	97	194	Y	6	5	0	0	0	0	6	5
71-71	3	S	.12000	98	195	Y	4	9	0	0	0	0	5	9
71-71	3	S	.12000	98	196	Y	3	8	0	0	0	0	3	10
71-71	3	S	.12000	99	197	Y	8	2	0	0	0	0	11	3
71-71	3	S	.12000	99	198	Y	7	8	0	0	0	0	7	9
71-71	3	S	.12000	100	199	Y	5	7	0	1	0	0	5	7
71-71	3	S	.12000	100	200	Y	3	7	1	1	0	0	3	11
71-71	3	S	1.20000	101	201	Y	4	7	1	0	0	0	6	7
71-71	3	S	1.20000	101	202	Y	4	4	0	0	0	0	4	5
71-71	3	S	1.20000	102	203	Y	5	6	0	0	0	0	5	6
71-71	3	S	1.20000	102	204	Y	8	5	0	0	0	0	8	5
71-71	3	S	1.20000	103	205	Y	5	3	0	0	0	0	6	4
71-71	3	S	1.20000	103	206	Y	7	4	0	0	0	0	7	4
71-71	3	S	1.20000	104	207	Y	3	9	0	0	0	0	4	9
71-71	3	S	1.20000	104	208	Y	4	6	0	0	0	0	4	8
71-71	3	S	1.20000	105	209	Y	4	7	0	0	0	0	4	7
71-71	3	S	1.20000	105	210	Y	3	8	0	0	0	0	3	8
71-71	3	S	1.20000	106	211	Y	5	9	0	0	0	0	6	8
71-71	3	S	1.20000	106	212	Y	6	8	0	0	0	0	3	10
71-71	3	S	1.20000	107	213	Y	2	10	0	0	0	0	8	7
71-71	3	S	1.20000	107	214	Y	6	5	0	0	0	0	1	2
71-71	3	S	1.20000	108	215	Y	3	10	0	0	0	0	3	10
71-71	3	S	1.20000	108	216	Y	6	7	1	0	0	0	6	7
71-71	3	S	1.20000	109	217	Y	4	7	1	0	0	0	4	7
71-71	3	S	1.20000	109	218	Y	6	5	0	0	0	0	6	6
71-71	3	S	1.20000	110	219	Y	4	6	0	0	0	0	4	6
71-71	3	S	1.20000	110	220	Y	7	3	1	0	0	0	7	4

DOMINANT LETHAL STUDY OF COMPOUND 71-71

MANGANESE SULFATE

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	R	L	R	L	R
TEM	3	S	.00020	11	21	Y	5	3	4	3	0	0	7	3
TEM	3	S	.00020	11	22	YY	4	2	4	2	0	0	7	2
TEM	3	S	.00020	12	23	YY	3	7	0	0	0	0	5	8
TEM	3	S	.00020	12	24	Y	6	5	6	4	0	0	5	6
TEM	3	S	.00020	13	25	YY	0	2	0	2	1	0	4	7
TEM	3	S	.00020	13	26	YY	8	4	6	2	0	0	5	6
TEM	3	S	.00020	14	27	YY	4	5	4	5	0	0	4	7
TEM	3	S	.00020	14	28	Y	1	2	0	0	0	0	7	6
TEM	3	S	.00020	15	29	YY	3	4	2	2	4	0	4	4
TEM	3	S	.00020	15	30	YY	4	6	2	5	5	1	5	7
TEM	3	S	.00020	16	31	YY	4	5	4	5	0	0	4	7
TEM	3	S	.00020	16	32	YY	5	3	5	3	0	0	4	7
TEM	3	S	.00020	17	33	YY	0	1	0	1	2	0	3	3
TEM	3	S	.00020	17	34	YY	3	2	3	2	0	0	6	5
TEM	3	S	.00020	18	35	YY	4	5	4	5	0	0	7	6
TEM	3	S	.00020	18	36	YY	2	1	2	1	0	0	7	6
TEM	3	S	.00020	19	37	YY	3	4	5	5	0	0	5	5
TEM	3	S	.00020	19	38	YY	5	5	5	5	0	0	6	5
TEM	3	S	.00020	20	39	YY	4	2	4	2	2	0	6	5
TEM	3	S	.00020	20	40	Y	3	8	2	4	0	1	3	9
CONTROL	3	M	0.00000	1	1	Y	3	0	0	0	0	0	3	8
CONTROL	3	M	0.00000	1	2	YY	5	8	0	0	0	0	5	8
CONTROL	3	M	0.00000	2	3	YY	7	5	0	0	0	0	7	5
CONTROL	3	M	0.00000	2	4	YY	7	8	0	0	0	0	7	6
CONTROL	3	M	0.00000	3	5	YY	6	0	1	0	0	0	6	4
CONTROL	3	M	0.00000	3	6	YY	10	3	1	0	0	0	10	3
CONTROL	3	M	0.00000	4	7	YY	7	6	0	0	0	0	8	6
CONTROL	3	M	0.00000	4	8	YY	6	7	0	0	0	0	6	7
CONTROL	3	M	0.00000	5	9	YY	10	3	3	2	0	0	10	4
CONTROL	3	M	0.00000	5	10	YY	4	9	0	1	0	0	5	9
CONTROL	3	M	0.00000	6	11	YY	3	9	0	0	1	0	3	9
CONTROL	3	M	0.00000	6	12	YY	4	5	2	0	0	0	5	6
CONTROL	3	M	0.00000	7	13	YY	5	7	0	0	0	0	5	7
CONTROL	3	M	0.00000	7	14	YY	6	8	0	0	0	0	6	8
CONTROL	3	M	0.00000	8	15	YY	7	4	0	0	0	0	7	5
CONTROL	3	M	0.00000	8	16	YY	7	5	0	0	0	0	5	6
CONTROL	3	M	0.00000	9	17	YY	5	9	0	0	0	1	7	6
CONTROL	3	M	0.00000	9	18	YY	7	6	1	1	0	0	1	0
CONTROL	3	M	0.00000	10	19	YY	10	4	1	1	0	0	10	4
CONTROL	3	M	0.00000	10	20	Y	6	4	0	0	0	0	8	4

DOMINANT LETHAL STUDY OF COMPOUND 71-71

MANGANESE SULFATE

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	R	L	R	L	R
71-71	3	M	.01200	71	141	Y	6	6	0	0	0	0	6	6
71-71	3	M	.01200	71	142	Y	4	7	1	0	0	0	5	7
71-71	3	M	.01200	72	143	Y	5	9	0	1	0	2	5	9
71-71	3	M	.01200	72	144	Y	6	4	2	3	0	0	7	4
71-71	3	M	.01200	73	145	N	0	0	0	0	0	0	0	0
71-71	3	M	.01200	73	146	Y	9	5	1	0	0	0	9	5
71-71	3	M	.01200	74	147	Y	8	8	0	2	0	0	10	8
71-71	3	M	.01200	74	148	Y	4	7	0	0	0	0	4	8
71-71	3	M	.01200	76	151	Y	5	4	0	0	0	0	5	4
71-71	3	M	.01200	76	152	Y	8	6	0	0	0	0	8	7
71-71	3	M	.01200	77	153	Y	6	4	0	0	0	0	6	4
71-71	3	M	.01200	77	154	Y	5	8	0	1	0	0	5	8
71-71	3	M	.01200	78	155	Y	7	6	1	0	0	0	7	6
71-71	3	M	.01200	78	156	Y	9	6	0	1	0	0	9	6
71-71	3	M	.01200	79	157	Y	8	4	1	2	1	0	8	4
71-71	3	M	.01200	79	158	Y	7	7	2	1	1	2	8	7
71-71	3	M	.01200	80	159	Y	7	4	0	1	1	0	9	4
71-71	3	M	.01200	80	160	Y	8	5	0	0	1	0	8	5
71-71	3	M	.12000	81	161	Y	8	4	0	0	0	0	8	6
71-71	3	M	.12000	81	162	Y	5	6	0	0	0	0	5	6
71-71	3	M	.12000	82	163	Y	9	5	1	0	0	0	9	5
71-71	3	M	.12000	82	164	Y	9	3	1	0	0	0	10	3
71-71	3	M	.12000	83	165	Y	7	5	0	1	0	0	7	5
71-71	3	M	.12000	83	166	Y	4	7	3	6	0	0	4	7
71-71	3	M	.12000	84	167	Y	7	7	0	0	0	0	7	7
71-71	3	M	.12000	84	168	Y	4	9	1	0	0	0	4	9
71-71	3	M	.12000	85	169	Y	0	2	0	1	0	0	0	0
71-71	3	M	.12000	85	170	Y	5	7	0	2	0	0	6	7
71-71	3	M	.12000	86	171	Y	4	8	0	1	0	0	4	8
71-71	3	M	.12000	86	172	Y	6	6	0	0	1	0	8	6
71-71	3	M	.12000	87	173	Y	4	10	0	0	0	0	4	10
71-71	3	M	.12000	87	174	Y	4	6	0	1	0	0	6	7
71-71	3	M	.12000	88	175	Y	6	5	1	0	0	0	8	5
71-71	3	M	.12000	88	176	Y	7	8	0	0	0	0	7	8
71-71	3	M	.12000	89	177	Y	7	5	0	0	1	0	7	6
71-71	3	M	.12000	89	178	Y	7	6	0	0	0	1	7	6
71-71	3	M	.12000	90	179	Y	5	6	0	0	1	0	6	6
71-71	3	M	.12000	90	180	Y	7	6	0	1	0	0	8	6

DOMINANT LETHAL STUDY OF COMPOUND 71-71

RANESE SULFATE

PAGE 15

TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.		IMPLANTS		EARLY DEATHS		LATE DEATHS		COMPOUNA LUTFA	
							L	H	L	K	L	K	L	H
71-71	3	M 1.20000	91	181	Y		6	6	0	0	0	1	7	7
71-71	3	M 1.20000	91	182	Y		2	2	0	0	0	0	9	4
71-71	3	M 1.20000	92	183	Y		4	9	0	0	0	0	5	10
71-71	3	M 1.20000	92	184	Y		6	8	0	0	0	1	8	8
71-71	3	M 1.20000	93	185	Y		9	4	1	0	0	0	9	4
71-71	3	M 1.20000	93	186	Y		7	6	0	0	0	0	7	6
71-71	3	M 1.20000	94	187	Y		6	6	0	0	0	0	6	8
71-71	3	M 1.20000	94	188	Y		3	7	0	0	0	0	3	8
71-71	3	M 1.20000	95	189	Y		8	7	0	0	0	0	8	10
71-71	3	M 1.20000	95	190	Y		11	4	1	0	0	0	11	4
71-71	3	M 1.20000	96	191	Y		7	5	0	0	0	0	7	6
71-71	3	M 1.20000	96	192	Y		8	3	0	0	0	1	9	4
71-71	3	M 1.20000	97	193	Y		5	5	0	0	0	0	6	6
71-71	3	M 1.20000	97	194	Y		5	5	0	0	0	0	7	5
71-71	3	M 1.20000	98	195	Y		3	6	0	0	1	0	7	6
71-71	3	M 1.20000	98	196	Y		9	6	0	0	0	0	9	6
71-71	3	M 1.20000	99	197	Y		8	5	0	0	0	0	8	5
71-71	3	M 1.20000	99	198	Y		5	5	0	0	0	0	6	5
71-71	3	M 1.20000	100	199	Y		4	9	0	0	0	0	4	9
71-71	3	M 1.20000	100	200	Y		7	5	0	0	0	0	7	5

DOMINANT LETHAL STUDY OF COMPOUND 71-71

MANGANESE SULFATE

PAGE 16

TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PHFG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	R	L	R
CONTROL	4	S 0.00000	1	1	Y	7	4	0	0	0	0	7 5
CONTROL	4	S 0.00000	1	2	Y	4	6	0	0	0	0	5 6
CONTROL	4	S 0.00000	2	3	Y	8	5	0	0	1	0	5 6
CONTROL	4	S 0.00000	2	4	Y	5	9	0	0	0	0	8 7
CONTROL	4	S 0.00000	3	5	YY	7	7	0	0	0	0	6 4
CONTROL	4	S 0.00000	3	6	YY	6	4	0	0	0	0	5 8
CONTROL	4	S 0.00000	4	7	YY	5	8	0	0	0	0	8 8
CONTROL	4	S 0.00000	4	8	YY	8	6	0	0	0	0	7 6
CONTROL	4	S 0.00000	5	9	YY	7	6	0	1	0	0	6 9
CONTROL	4	S 0.00000	5	10	YY	4	8	0	0	0	0	4 5
CONTROL	4	S 0.00000	6	11	YY	1	3	0	0	0	0	4 9
CONTROL	4	S 0.00000	6	12	YY	4	9	0	1	0	0	7 8
CONTROL	4	S 0.00000	7	13	YY	7	8	0	1	0	0	7 5
CONTROL	4	S 0.00000	7	14	YY	7	5	1	0	0	0	10 4
CONTROL	4	S 0.00000	8	15	YY	10	3	0	2	0	0	3 8
CONTROL	4	S 0.00000	8	16	YY	3	8	0	0	0	0	4 7
CONTROL	4	S 0.00000	9	17	YY	4	7	0	1	0	0	5 4
CONTROL	4	S 0.00000	9	18	YY	5	4	0	0	0	0	3 9
CONTROL	4	S 0.00000	10	19	YY	3	9	0	0	0	0	6 5
CONTROL	4	S 0.00000	10	20	Y	6	5	0	0	0	0	6 6
71-71	4	S .01200	81	161	Y	5	9	1	0	0	0	5 9
71-71	4	S .01200	81	162	YY	4	7	0	0	0	0	4 7
71-71	4	S .01200	82	163	YY	6	6	0	1	0	0	8 5
71-71	4	S .01200	82	164	YY	8	5	0	0	0	0	10 3
71-71	4	S .01200	83	165	YY	5	5	0	0	1	1	8 8
71-71	4	S .01200	83	166	YY	7	3	0	0	0	0	8 6
71-71	4	S .01200	84	167	YY	7	6	0	1	0	0	5 7
71-71	4	S .01200	84	168	YY	5	7	0	0	0	0	8 6
71-71	4	S .01200	85	169	YY	8	6	2	0	0	0	8 6
71-71	4	S .01200	85	170	YY	7	5	0	0	1	0	9 4
71-71	4	S .01200	86	171	YY	8	4	0	1	0	0	7 4
71-71	4	S .01200	86	172	YY	7	4	0	0	1	0	5 7
71-71	4	S .01200	87	173	YY	5	7	0	0	0	0	4 9
71-71	4	S .01200	87	174	YY	4	8	0	0	0	0	4 5
71-71	4	S .01200	88	175	YY	9	4	0	0	0	0	8 6
71-71	4	S .01200	88	176	YY	8	5	0	1	0	0	4 6
71-71	4	S .01200	89	177	YY	4	6	1	4	0	2	6 5
71-71	4	S .01200	89	178	YY	5	7	0	0	0	0	7 6
71-71	4	S .01200	90	179	YY	7	6	0	1	0	0	7 6
71-71	4	S .01200	90	180	Y							

DOMINANT LETHAL STUDY OF COMPOUND 71-71

MANGANESE SULFATE

PAGE 17

TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	R	L	R	L	R
71-71	4	S	.12000	91	181	Y	4	7	0	0	0	0	5	7
71-71	4	S	.12000	91	182	YY	4	7	0	0	0	0	4	8
71-71	4	S	.12000	92	183	YY	7	8	0	0	0	0	7	8
71-71	4	S	.12000	92	184	Y	5	8	1	0	0	0	5	9
71-71	4	S	.12000	93	185	YY	5	6	0	0	0	0	6	8
71-71	4	S	.12000	93	186	YY	6	0	0	0	0	0	8	6
71-71	4	S	.12000	94	187	YY	4	9	0	0	0	0	4	9
71-71	4	S	.12000	94	188	YY	7	9	1	1	0	0	7	9
71-71	4	S	.12000	95	189	YY	4	8	0	0	0	0	4	8
71-71	4	S	.12000	95	190	YY	5	8	0	0	0	0	5	8
71-71	4	S	.12000	96	191	YY	6	9	1	4	0	0	6	9
71-71	4	S	.12000	96	192	YY	6	7	0	0	0	0	6	7
71-71	4	S	.12000	97	193	YY	4	8	0	2	0	0	7	8
71-71	4	S	.12000	97	194	YY	7	7	1	1	0	0	10	7
71-71	4	S	.12000	98	195	YY	10	5	1	0	0	0	10	5
71-71	4	S	.12000	98	196	YY	7	6	1	0	0	0	7	6
71-71	4	S	.12000	99	197	YY	3	10	0	0	0	0	3	10
71-71	4	S	.12000	99	198	YY	7	9	0	0	0	0	7	9
71-71	4	S	.12000	100	199	YY	10	4	0	0	0	0	11	4
71-71	4	S	.12000	100	200	Y								
71-71	4	S	1.20000	101	201	Y	4	9	0	0	0	0	4	9
71-71	4	S	1.20000	101	202	YY	5	8	0	1	0	0	6	8
71-71	4	S	1.20000	102	203	YY	3	6	0	0	0	0	4	6
71-71	4	S	1.20000	102	204	YY	4	6	0	0	0	0	9	7
71-71	4	S	1.20000	103	205	YY	9	7	0	0	0	0	9	6
71-71	4	S	1.20000	103	206	YY	8	5	0	0	0	0	6	8
71-71	4	S	1.20000	104	207	YY	6	7	0	0	0	0	7	8
71-71	4	S	1.20000	104	208	YY	7	8	0	0	1	3	3	8
71-71	4	S	1.20000	105	209	YY	3	7	0	0	0	0	5	7
71-71	4	S	1.20000	105	210	YY	4	7	0	0	0	0	3	9
71-71	4	S	1.20000	106	211	YY	3	9	0	2	0	0	5	10
71-71	4	S	1.20000	106	212	YY	5	9	0	0	1	0	4	8
71-71	4	S	1.20000	107	213	YY	4	7	0	0	0	0	7	5
71-71	4	S	1.20000	107	214	YY	7	5	0	0	0	0	3	11
71-71	4	S	1.20000	108	215	YY	3	11	0	0	0	0	6	7
71-71	4	S	1.20000	108	216	YY	6	7	0	0	0	0	4	6
71-71	4	S	1.20000	109	217	YY	5	6	0	1	0	0	6	5
71-71	4	S	1.20000	109	218	YY	4	6	0	0	0	0	6	5
71-71	4	S	1.20000	110	219	YY	6	5	1	1	3	2	0	7
71-71	4	S	1.20000	110	220	Y	5	7	1	1	3	2	0	

DOMINANT LETHAL STUDY OF COMPOUND 71-

MANGANESE SULFATE

PAGE 1H

TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PRFG.	IMPLANTS L	IMPLANTS R	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
									L	R	L	R	L	R
TEM	4	S	.00020	11	21	YY	6	7	4	1	0	1	7	7
TEM	4	S	.00020	11	22	YY	1	3	1	3	0	0	8	9
TEM	4	S	.00020	12	23	YY	2	2	2	2	0	4	8	5
TEM	4	S	.00020	12	24	YY	4	2	0	2	0	4	0	4
TEM	4	S	.00020	13	25	YY	0	2	0	2	2	0	0	5
TEM	4	S	.00020	13	26	YY	3	3	3	3	0	0	0	5
TEM	4	S	.00020	14	27	YN	0	0	0	0	0	0	0	6
TEM	4	S	.00020	14	28	YY	0	2	0	2	2	0	0	6
TEM	4	S	.00020	15	29	YY	3	2	3	3	2	2	0	8
TEM	4	S	.00020	15	30	YY	2	3	2	0	0	0	0	0
TEM	4	S	.00020	16	31	YY	0	3	4	3	0	0	0	8
TEM	4	S	.00020	16	32	YY	5	3	1	1	0	0	0	3
TEM	4	S	.00020	17	33	YY	1	5	5	5	0	0	0	6
TEM	4	S	.00020	17	34	YY	5	5	5	5	0	0	0	6
TEM	4	S	.00020	18	35	YY	2	4	2	2	0	0	0	8
TEM	4	S	.00020	18	36	YY	2	2	1	1	0	0	0	6
TEM	4	S	.00020	19	37	YN	0	0	0	0	0	0	0	4
TEM	4	S	.00020	19	38	YY	2	4	1	4	0	0	0	7
TEM	4	S	.00020	20	39	YY	3	5	3	5	0	0	0	5
TEM	4	S	.00020	20	40	Y	4	3	3	2	0	0	0	6
CONTROL	4	M	0.00000	1	1	YY	7	4	0	0	1	2	0	4
CONTROL	4	M	0.00000	1	2	YY	0	1	0	0	0	1	0	7
CONTROL	4	M	0.00000	2	3	YY	7	3	0	1	0	0	0	5
CONTROL	4	M	0.00000	2	4	YY	3	0	0	0	0	0	0	6
CONTROL	4	M	0.00000	3	5	YY	10	6	0	0	1	0	0	10
CONTROL	4	M	0.00000	3	6	YY	5	7	0	0	1	0	0	5
CONTROL	4	M	0.00000	4	7	YY	8	5	0	0	0	0	0	8
CONTROL	4	M	0.00000	4	8	YY	7	4	0	0	0	0	0	4
CONTROL	4	M	0.00000	5	9	YY	7	7	0	0	0	0	0	7
CONTROL	4	M	0.00000	5	10	YY	4	9	0	0	0	0	0	8
CONTROL	4	M	0.00000	6	11	YY	5	8	0	0	0	0	0	6
CONTROL	4	M	0.00000	6	12	YY	5	7	0	0	0	0	0	7
CONTROL	4	M	0.00000	7	13	YY	8	7	0	0	0	0	0	12
CONTROL	4	M	0.00000	7	14	YY	9	7	1	1	0	0	0	9
CONTROL	4	M	0.00000	8	15	YY	10	5	1	1	0	0	0	5
CONTROL	4	M	0.00000	8	16	YY	5	9	0	0	0	0	0	6
CONTROL	4	M	0.00000	9	17	YY	11	4	2	0	0	0	0	14
CONTROL	4	M	0.00000	9	18	YY	8	13	5	6	0	0	0	10
CONTROL	4	M	0.00000	10	19	YY	5	6	1	1	0	0	0	7
CONTROL	4	M	0.00000	10	20	Y	2	10	0	0	0	0	0	14

DOMINANT LETHAL STUDY OF COMPOUND 71-71

MANGANESE SULFATE

PAGE 19

TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	H	L	H	L	H
71-71	4	M	.01200	71	141	Y	8	6	0	1	0	1	8	7
71-71	4	M	.01200	71	142	Y	6	7	0	0	1	6	7	7
71-71	4	M	.01200	72	143	Y	5	6	0	0	0	0	8	6
71-71	4	M	.01200	72	144	Y	1	0	0	0	1	0	10	11
71-71	4	M	.01200	73	145	Y	7	8	6	6	0	1	8	9
71-71	4	M	.01200	73	146	Y	10	4	0	1	0	0	10	5
71-71	4	M	.01200	74	147	Y	8	6	0	0	0	0	8	6
71-71	4	M	.01200	74	148	Y	8	5	0	0	0	0	9	6
71-71	4	M	.01200	76	151	Y	7	7	1	0	0	0	7	7
71-71	4	M	.01200	76	152	Y	5	8	0	0	0	0	6	9
71-71	4	M	.01200	77	153	Y	6	2	0	0	0	0	7	6
71-71	4	M	.01200	77	154	Y	3	8	0	1	0	0	4	9
71-71	4	M	.01200	78	155	Y	4	11	0	1	0	0	4	12
71-71	4	M	.01200	78	156	Y	4	7	1	3	1	0	4	8
71-71	4	M	.01200	79	157	Y	10	5	2	0	0	0	10	5
71-71	4	M	.01200	79	158	Y	5	10	1	1	0	0	6	10
71-71	4	M	.01200	80	159	Y	8	5	0	0	0	0	9	5
71-71	4	M	.01200	80	160	Y	7	5	1	0	0	0	7	7
71-71	4	M	.12000	81	161	Y	7	5	1	0	0	0	7	7
71-71	4	M	.12000	81	162	Y	6	9	0	2	0	1	6	9
71-71	4	M	.12000	82	163	Y	5	10	0	1	0	0	5	10
71-71	4	M	.12000	82	164	Y	6	6	0	0	0	0	6	8
71-71	4	M	.12000	83	165	Y	9	6	1	1	0	0	4	10
71-71	4	M	.12000	83	166	Y	4	10	0	0	0	0	10	10
71-71	4	M	.12000	84	167	Y	0	1	0	0	0	0	5	8
71-71	4	M	.12000	84	168	Y	5	7	0	0	0	0	8	3
71-71	4	M	.12000	85	169	Y	6	3	1	1	0	0	6	8
71-71	4	M	.12000	85	170	Y	5	8	1	1	0	0	7	8
71-71	4	M	.12000	86	171	Y	7	8	0	1	0	0	8	5
71-71	4	M	.12000	86	172	Y	8	5	0	1	0	0	7	5
71-71	4	M	.12000	87	173	Y	7	7	0	0	0	0	7	8
71-71	4	M	.12000	87	174	Y	6	7	0	0	0	0	6	7
71-71	4	M	.12000	88	175	Y	6	9	0	1	0	0	6	9
71-71	4	M	.12000	88	176	Y	6	5	0	0	0	0	7	5
71-71	4	M	.12000	89	177	Y	7	5	0	0	0	0	7	5
71-71	4	M	.12000	89	178	Y	5	8	0	0	0	0	7	5
71-71	4	M	.12000	90	179	Y	7	5	0	0	0	0	7	5
71-71	4	M	.12000	90	180	Y	7	5	0	0	0	0	7	5

DOMINANT LETHAL STUDY OF COMPOUND 71-71

MANGANESE SULFATE

PAGE 20

TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PRFG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	H	L	R
71-71	4	M 1.20000	91	181	Y	5	9	0	0	1	0	5 10
71-71	4	M 1.20000	91	182	Y	7	6	0	0	0	1	8 6
71-71	4	M 1.20000	92	183	Y	7	6	0	0	0	1	7 6
71-71	4	M 1.20000	92	184	Y	5	9	1	0	0	0	5 9
71-71	4	M 1.20000	93	185	Y	5	7	0	0	0	0	6 7
71-71	4	M 1.20000	93	186	Y	7	6	0	0	0	0	7 6
71-71	4	M 1.20000	94	187	Y	8	5	1	1	0	0	8 5
71-71	4	M 1.20000	94	188	Y	5	8	0	0	0	0	5 8
71-71	4	M 1.20000	95	189	Y	7	5	0	0	0	0	8 5
71-71	4	M 1.20000	95	190	Y	6	7	1	0	0	0	6 9
71-71	4	M 1.20000	96	191	Y	7	5	0	0	0	0	7 5
71-71	4	M 1.20000	96	192	N	6	0	0	0	0	0	0 0
71-71	4	M 1.20000	97	193	Y	8	6	1	0	0	0	8 6
71-71	4	M 1.20000	97	194	Y	7	4	0	0	0	0	10 5
71-71	4	M 1.20000	98	195	Y	7	7	0	1	0	0	7 7
71-71	4	M 1.20000	98	196	Y	5	7	0	4	0	0	7 7
71-71	4	M 1.20000	99	197	Y	8	7	0	0	0	0	8 7
71-71	4	M 1.20000	99	198	Y	6	8	0	0	0	0	6 8
71-71	4	M 1.20000	100	199	Y	12	4	0	0	0	0	12 4
71-71	4	M 1.20000	100	200	Y	6	6	0	0	0	0	6 6

DOMINANT LETHAL STUDY OF COMPOUND 71-71

MOLYBDENUM SULFATE

PAGE 21

TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CONFORMA LUTEA	
						L	R	L	R	L	R	L	R
CONTROL	5	S 0.00000	1	1	Y	5	9	2	1	0	0	6	9
CONTROL	5	S 0.00000	1	2	YY	4	2	0	0	0	0	6	5
CONTROL	5	S 0.00000	2	3	YY	9	6	0	0	0	0	9	6
CONTROL	5	S 0.00000	2	4	YY	5	10	0	0	0	1	5	10
CONTROL	5	S 0.00000	3	5	YY	8	5	0	0	0	0	5	9
CONTROL	5	S 0.00000	3	6	YY	5	9	0	0	0	0	4	11
CONTROL	5	S 0.00000	4	7	YY	4	11	0	0	1	1	5	9
CONTROL	5	S 0.00000	4	8	YY	5	8	0	0	0	0	7	4
CONTROL	5	S 0.00000	5	9	YY	7	3	0	0	0	0	7	6
CONTROL	5	S 0.00000	5	10	YY	7	6	0	1	0	0	7	4
CONTROL	5	S 0.00000	6	11	YY	8	4	0	0	0	0	8	4
CONTROL	5	S 0.00000	6	12	YY	5	8	0	0	1	3	7	10
CONTROL	5	S 0.00000	7	13	YY	4	9	0	0	0	0	7	7
CONTROL	5	S 0.00000	7	14	YY	7	7	0	0	0	1	4	9
CONTROL	5	S 0.00000	8	15	YY	3	8	0	0	0	0	7	7
CONTROL	5	S 0.00000	8	16	YY	7	7	1	1	0	0	5	10
CONTROL	5	S 0.00000	9	17	YY	5	10	1	1	0	0	8	3
CONTROL	5	S 0.00000	9	18	YY	1	0	0	0	0	0	6	6
CONTROL	5	S 0.00000	10	19	YY	6	5	1	2	0	0	7	7
CONTROL	5	S 0.00000	10	20	Y	7	7	2	2	0	0	7	7
71-71	5	S .01200	81	161	Y	3	11	0	0	0	0	3	11
71-71	5	S .01200	81	162	YY	7	7	0	0	0	0	7	7
71-71	5	S .01200	82	163	YY	6	8	1	0	0	0	6	8
71-71	5	S .01200	82	164	YY	5	8	0	0	0	0	5	8
71-71	5	S .01200	83	165	YY	8	4	1	1	0	0	9	4
71-71	5	S .01200	83	166	YY	8	5	0	0	0	0	8	5
71-71	5	S .01200	84	167	YY	5	9	0	0	0	0	5	10
71-71	5	S .01200	84	168	YY	9	3	3	1	1	0	9	3
71-71	5	S .01200	85	169	YY	7	5	2	1	0	0	7	5
71-71	5	S .01200	85	170	YY	6	7	4	1	0	0	6	7
71-71	5	S .01200	86	171	YY	3	8	0	0	0	0	3	8
71-71	5	S .01200	86	172	YY	8	8	0	0	0	0	3	11
71-71	5	S .01200	87	173	YY	3	11	0	0	1	0	5	5
71-71	5	S .01200	87	174	YY	5	5	0	0	2	0	6	7
71-71	5	S .01200	88	175	YY	6	7	0	0	0	0	3	9
71-71	5	S .01200	88	176	YY	3	9	0	0	0	0	6	8
71-71	5	S .01200	89	177	YY	6	8	0	0	0	0	6	6
71-71	5	S .01200	89	178	YY	4	5	0	0	0	0	8	7
71-71	5	S .01200	90	179	YY	6	3	0	0	0	1	5	7
71-71	5	S .01200	90	180	Y	5	7	0	0	0	0	7	7

DOMINANT LETHAL STUDY OF COMPOUND 71-71

MANGANESE SULFATE

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORAL LUTEA		
								L	R	L	R	L	R	
TEM	5	S	.00020	11	21	Y	6	6	0	1	0	0	6	6
TEM	5	S	.00020	11	22	YY	7	3	0	1	1	0	8	5
TEM	5	S	.00020	12	23	YY	6	5	0	0	0	2	6	8
TEM	5	S	.00020	12	24	YY	5	8	1	0	0	0	6	6
TEM	5	S	.00020	13	25	YY	6	0	1	0	0	0	6	10
TEM	5	S	.00020	13	26	YY	3	3	3	1	2	0	4	8
TEM	5	S	.00020	14	27	YY	3	8	1	2	1	0	6	7
TEM	5	S	.00020	14	28	YY	6	7	2	2	1	0	5	8
TEM	5	S	.00020	15	29	YY	5	8	0	0	0	0	5	10
TEM	5	S	.00020	15	30	YY	5	4	0	3	1	0	4	5
TEM	5	S	.00020	16	31	YY	9	5	0	0	0	0	9	9
TEM	5	S	.00020	16	32	YY	9	5	0	0	0	0	5	4
TEM	5	S	.00020	17	33	YY	4	6	4	1	0	0	4	5
TEM	5	S	.00020	17	34	YY	4	9	2	3	0	0	4	5
TEM	5	S	.00020	18	35	YY	3	7	6	6	0	0	3	7
TEM	5	S	.00020	18	36	YY	9	5	0	1	0	0	8	5
TEM	5	S	.00020	19	37	YY	8	3	0	2	0	0	5	5
TEM	5	S	.00020	19	38	YY	5	5	0	2	0	0	8	8
TEM	5	S	.00020	20	39	YY	5	7	0	1	0	0	5	3
TEM	5	S	.00020	20	40	YY	7	2	1	4	0	1	8	3
CONTROL	5	M	0.00000	1	1	Y	9	6	0	0	0	0	9	6
CONTROL	5	M	0.00000	1	2	YY	2	2	0	0	0	0	8	3
CONTROL	5	M	0.00000	2	3	YY	8	7	0	0	0	0	8	7
CONTROL	5	M	0.00000	2	4	YY	5	9	0	0	0	0	6	9
CONTROL	5	M	0.00000	3	5	YY	7	5	0	0	0	0	8	5
CONTROL	5	M	0.00000	3	6	YY	7	4	0	0	0	0	8	4
CONTROL	5	M	0.00000	4	7	YY	10	5	0	0	0	0	10	7
CONTROL	5	M	0.00000	4	8	YY	9	5	0	0	0	0	8	5
CONTROL	5	M	0.00000	5	9	YY	7	6	0	1	0	0	10	6
CONTROL	5	M	0.00000	5	10	YY	5	11	0	0	0	0	11	11
CONTROL	5	M	0.00000	6	11	YY	2	0	0	0	0	0	6	6
CONTROL	5	M	0.00000	6	12	YY	4	9	0	0	0	0	9	9
CONTROL	5	M	0.00000	7	13	YY	10	4	0	4	0	0	11	8
CONTROL	5	M	0.00000	7	14	YY	0	2	0	0	0	0	8	6
CONTROL	5	M	0.00000	8	15	NN	0	0	0	0	0	0	0	0
CONTROL	5	M	0.00000	8	16	YY	0	0	0	0	0	0	0	0
CONTROL	5	M	0.00000	9	17	YY	6	7	0	0	0	0	6	7
CONTROL	5	M	0.00000	9	18	YY	9	6	0	0	0	0	9	6
CONTROL	5	M	0.00000	10	19	YY	7	7	0	0	0	0	7	8
CONTROL	5	M	0.00000	10	20	YY	6	6	0	0	0	0	7	7

DOMINANT LETHAL STUDY OF COMPOUND 71-71

MANGANESE SULFATE

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	R	L	R	L	R
71-71	5	M	.01200	71	141	Y	5	8	0	0	0	1	5	8
71-71	5	M	.01200	71	142	Y	6	9	1	0	0	0	7	10
71-71	5	M	.01200	72	143	Y	6	6	0	0	0	0	7	6
71-71	5	M	.01200	72	144	Y	0	3	0	1	0	0	4	6
71-71	5	M	.01200	73	145	Y	4	11	0	3	0	0	4	12
71-71	5	M	.01200	73	146	Y	6	4	0	1	0	0	6	4
71-71	5	M	.01200	74	147	Y	8	6	0	0	0	1	8	6
71-71	5	M	.01200	74	148	Y	5	8	0	0	0	0	5	8
71-71	5	M	.01200	76	151	Y	6	7	4	5	1	0	6	8
71-71	5	M	.01200	76	152	Y	7	5	0	0	0	0	7	6
71-71	5	M	.01200	77	153	Y	7	4	1	1	0	0	8	4
71-71	5	M	.01200	77	154	Y	1	1	0	0	0	0	10	3
71-71	5	M	.01200	78	155	Y	3	9	0	0	0	0	3	9
71-71	5	M	.01200	78	156	Y	6	4	0	0	0	0	6	4
71-71	5	M	.01200	79	157	Y	7	5	0	0	0	0	7	5
71-71	5	M	.01200	79	158	Y	5	7	0	1	0	0	5	8
71-71	5	M	.01200	80	159	Y	9	0	1	0	4	0	10	3
71-71	5	M	.01200	80	160	Y	4	9	0	0	0	0	11	13
71-71	5	M	.12000	81	161	Y	9	3	5	2	0	0	15	5
71-71	5	M	.12000	81	162	Y	4	8	0	0	0	0	5	8
71-71	5	M	.12000	82	163	Y	8	2	0	0	0	0	8	2
71-71	5	M	.12000	82	164	Y	8	4	1	0	1	0	9	4
71-71	5	M	.12000	83	165	Y	5	6	0	0	0	0	5	6
71-71	5	M	.12000	83	166	Y	7	1	0	0	0	0	7	5
71-71	5	M	.12000	84	167	Y	4	1	4	1	0	0	9	4
71-71	5	M	.12000	84	168	Y	6	6	0	0	0	0	7	6
71-71	5	M	.12000	85	169	Y	2	8	0	0	0	0	3	10
71-71	5	M	.12000	85	170	Y	4	11	0	2	0	0	4	12
71-71	5	M	.12000	86	171	Y	7	6	0	0	0	0	7	6
71-71	5	M	.12000	86	172	Y	7	3	0	1	0	0	8	5
71-71	5	M	.12000	87	173	Y	6	6	1	0	0	0	8	6
71-71	5	M	.12000	87	174	Y	8	5	1	0	0	0	8	5
71-71	5	M	.12000	88	175	Y	8	6	0	0	0	0	8	7
71-71	5	M	.12000	88	176	Y	4	9	0	1	0	0	6	9
71-71	5	M	.12000	89	177	Y	6	6	0	0	0	0	6	8
71-71	5	M	.12000	89	178	Y	6	1	0	0	1	0	6	8
71-71	5	M	.12000	90	179	Y	6	5	1	0	0	0	8	5
71-71	5	M	.12000	90	180	Y	6	9	0	0	0	0	6	9

DOMINANT LETHAL STUDY OF COMPOUND 71-71

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA		
							L	R	L	H	L	H	
71-71	5	M 1.20000	91	181	Y	6	6	0	0	0	0	7	8
71-71	5	M 1.20000	91	182	YY	7	5	0	0	0	0	7	5
71-71	5	M 1.20000	92	183	YY	6	7	0	0	0	0	7	7
71-71	5	M 1.20000	92	184	YY	7	5	1	1	0	0	7	5
71-71	5	M 1.20000	93	185	YY	6	8	0	0	0	0	7	8
71-71	5	M 1.20000	93	186	YY	7	7	0	0	0	0	7	7
71-71	5	M 1.20000	94	187	YY	4	8	0	0	0	0	5	8
71-71	5	M 1.20000	94	188	YY	9	4	1	0	0	0	9	4
71-71	5	M 1.20000	95	189	YY	5	4	0	0	0	0	7	5
71-71	5	M 1.20000	95	190	YY	9	8	0	1	0	0	10	10
71-71	5	M 1.20000	96	191	YY	4	5	1	0	0	0	6	5
71-71	5	M 1.20000	96	192	YY	7	6	1	1	0	0	7	6
71-71	5	M 1.20000	97	193	YY	8	6	0	1	0	0	9	7
71-71	5	M 1.20000	97	194	YY	8	4	2	0	0	0	8	4
71-71	5	M 1.20000	98	195	YY	4	9	0	0	0	0	4	9
71-71	5	M 1.20000	98	196	YY	5	6	0	0	0	0	6	6
71-71	5	M 1.20000	99	197	YY	10	3	1	0	0	0	11	5
71-71	5	M 1.20000	99	198	YY	4	10	0	0	0	0	4	10
71-71	5	M 1.20000	100	199	YY	6	7	3	2	0	0	7	7
71-71	5	M 1.20000	100	200	Y	11	4	1	0	0	0	12	6

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PAGE 24

TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PKFG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA		
								L	R	L	R	L	R	
CONTROL	6	S	0.00000	1	1	YY	4	5	0	0	0	0	6	5
CONTROL	6	S	0.00000	1	2	YY	5	3	0	1	0	0	5	6
CONTROL	6	S	0.00000	2	3	YY	6	7	1	1	1	0	8	8
CONTROL	6	S	0.00000	2	4	YY	6	2	1	0	1	0	4	8
CONTROL	6	S	0.00000	3	5	YY	3	6	0	0	0	0	6	5
CONTROL	6	S	0.00000	3	6	YY	6	6	1	1	0	0	6	6
CONTROL	6	S	0.00000	4	7	YY	5	9	0	0	0	0	6	6
CONTROL	6	S	0.00000	4	8	YY	6	5	0	0	0	0	6	6
CONTROL	6	S	0.00000	5	9	YY	6	5	1	1	0	0	7	5
CONTROL	6	S	0.00000	5	10	YY	7	4	0	0	0	0	6	4
CONTROL	6	S	0.00000	6	11	YY	6	4	0	0	0	0	7	4
CONTROL	6	S	0.00000	6	12	YY	7	5	0	0	0	0	6	6
CONTROL	6	S	0.00000	7	13	YY	4	6	0	0	0	0	5	9
CONTROL	6	S	0.00000	7	14	YY	5	8	0	0	0	0	6	7
CONTROL	6	S	0.00000	8	15	YY	8	6	0	0	0	0	5	5
CONTROL	6	S	0.00000	8	16	YY	4	7	0	0	1	0	3	7
CONTROL	6	S	0.00000	9	17	YY	3	8	0	0	0	0	8	6
CONTROL	6	S	0.00000	9	18	YY	8	6	0	0	0	0	6	8
CONTROL	6	S	0.00000	10	19	YY	5	8	1	0	1	0	4	4
CONTROL	6	S	0.00000	10	20	YY	10	4	0	0	0	0	10	4
71-71	6	S	.01200	81	161	YY	3	7	2	3	0	0	6	14
71-71	6	S	.01200	81	162	YY	4	6	0	0	0	0	4	6
71-71	6	S	.01200	82	163	YY	8	4	1	0	0	0	8	6
71-71	6	S	.01200	82	164	YY	7	8	0	0	0	0	7	9
71-71	6	S	.01200	83	165	YY	2	0	0	0	0	0	3	8
71-71	6	S	.01200	83	166	YY	6	8	0	0	0	0	6	8
71-71	6	S	.01200	84	167	YY	6	7	1	0	0	0	7	9
71-71	6	S	.01200	84	168	YY	7	8	0	0	0	0	7	6
71-71	6	S	.01200	85	169	YY	1	6	0	0	0	0	5	7
71-71	6	S	.01200	85	170	YY	5	6	0	0	1	0	3	5
71-71	6	S	.01200	86	171	YY	7	5	0	0	1	0	3	8
71-71	6	S	.01200	86	172	YY	3	8	0	0	0	0	6	5
71-71	6	S	.01200	87	173	YY	6	8	0	0	0	0	6	5
71-71	6	S	.01200	87	174	YY	6	5	0	0	0	0	6	8
71-71	6	S	.01200	88	175	YY	3	4	0	0	0	0	7	11
71-71	6	S	.01200	88	176	YY	4	7	1	0	0	0	4	7
71-71	6	S	.01200	89	177	YY	7	6	0	0	0	0	8	8
71-71	6	S	.01200	89	178	YY	6	8	0	0	0	0	6	10
71-71	6	S	.01200	90	179	YY	7	7	0	0	0	0	7	7
71-71	6	S	.01200	90	180	YY	7	7	0	0	0	0	7	7

TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	H	L	H	L	H
71-71	6	S	.12000	91	181	Y	5	6	1	0	0	0	6	6
71-71	6	S	.12000	91	182	Y	6	7	0	0	0	0	8	7
71-71	6	S	.12000	92	183	Y	1	7	0	0	0	0	2	8
71-71	6	S	.12000	92	184	Y	5	6	0	0	0	0	5	6
71-71	6	S	.12000	93	185	Y	6	8	0	0	0	0	6	8
71-71	6	S	.12000	93	186	Y	7	5	0	0	0	0	7	5
71-71	6	S	.12000	94	187	Y	4	7	0	0	1	0	9	9
71-71	6	S	.12000	94	188	Y	3	7	0	0	0	0	4	7
71-71	6	S	.12000	95	189	Y	6	5	0	0	0	0	7	7
71-71	6	S	.12000	95	190	Y	6	6	0	0	0	0	6	6
71-71	6	S	.12000	96	191	Y	3	8	0	0	0	0	4	8
71-71	6	S	.12000	96	192	Y	5	6	0	0	1	1	7	10
71-71	6	S	.12000	97	193	Y	7	5	0	0	0	0	7	5
71-71	6	S	.12000	97	194	Y	5	7	0	0	0	0	5	9
71-71	6	S	.12000	98	195	Y	7	4	0	0	0	0	7	5
71-71	6	S	.12000	98	196	Y	9	3	0	0	1	0	10	3
71-71	6	S	.12000	99	197	Y	8	2	0	0	0	0	8	2
71-71	6	S	.12000	99	198	Y	6	6	0	0	0	1	6	7
71-71	6	S	.12000	100	199	Y	7	6	0	1	0	0	7	7
71-71	6	S	.12000	100	200	Y	3	9	0	0	0	0	5	9
71-71	6	S	1.20000	101	201	Y	7	6	0	0	0	0	7	6
71-71	6	S	1.20000	101	202	Y	6	5	0	0	0	0	7	5
71-71	6	S	1.20000	102	203	Y	7	7	0	0	0	0	8	7
71-71	6	S	1.20000	102	204	Y	10	4	0	0	1	1	10	4
71-71	6	S	1.20000	103	205	Y	11	3	0	0	0	0	12	3
71-71	6	S	1.20000	103	206	Y	9	6	1	1	1	0	9	6
71-71	6	S	1.20000	104	207	Y	6	9	0	0	0	0	6	9
71-71	6	S	1.20000	104	208	Y	6	9	0	0	0	0	6	9
71-71	6	S	1.20000	105	209	Y	5	7	0	0	0	0	6	7
71-71	6	S	1.20000	105	210	Y	2	3	0	0	0	0	7	7
71-71	6	S	1.20000	106	211	Y	6	9	0	1	0	0	7	9
71-71	6	S	1.20000	106	212	Y	5	8	0	0	0	0	5	8
71-71	6	S	1.20000	107	213	Y	8	6	0	0	0	0	8	6
71-71	6	S	1.20000	107	214	Y	1	1	1	1	0	0	1	1
71-71	6	S	1.20000	108	215	Y	3	6	0	0	0	0	3	7
71-71	6	S	1.20000	108	216	Y	3	8	0	0	0	0	3	8
71-71	6	S	1.20000	109	217	Y	6	4	0	1	0	0	6	4
71-71	6	S	1.20000	109	218	Y	4	6	0	0	0	0	5	6
71-71	6	S	1.20000	110	219	Y	7	6	0	0	0	0	8	6
71-71	6	S	1.20000	110	220	Y	6	8	0	2	0	0	6	8

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MANGANESE SULFATE

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PKFG.	IMPLANTS	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA		
							L	R	L	H	L	H	
TEM	6	S .00020	11	21	Y	4	H	0	0	0	0	4	H
TEM	6	S .00020	11	22	Y	8	A	0	0	0	0	8	6
TEM	6	S .00020	12	23	Y	6	6	1	1	0	0	7	6
TEM	6	S .00020	12	24	Y	3	A	0	0	1	0	3	8
TEM	6	S .00020	13	25	Y	6	7	0	0	0	0	6	8
TEM	6	S .00020	14	27	Y	8	6	0	0	0	0	8	7
TEM	6	S .00020	14	28	Y	7	7	0	0	0	0	8	7
TEM	6	S .00020	15	29	Y	5	6	0	0	0	0	5	6
TEM	6	S .00020	15	30	Y	8	7	0	0	0	0	3	6
TEM	6	S .00020	16	31	Y	3	5	0	0	0	0	6	6
TEM	6	S .00020	16	32	Y	6	6	0	0	0	0	6	7
TEM	6	S .00020	17	33	Y	6	7	1	1	0	0	6	7
TEM	6	S .00020	17	34	Y	7	5	0	0	0	0	8	8
TEM	6	S .00020	18	35	Y	4	10	0	1	0	0	4	10
TEM	6	S .00020	18	36	Y	6	6	0	0	0	0	6	6
TEM	6	S .00020	19	37	Y	8	4	0	0	0	0	8	4
TEM	6	S .00020	19	38	Y	6	8	0	0	0	0	6	8
TEM	6	S .00020	20	39	Y	3	9	0	0	0	0	3	11
TEM	6	S .00020	20	40	Y	7	8	0	0	0	0	7	9
CONTROL	6	M 0.00000	1	1	Y	4	8	0	0	0	0	5	8
CONTROL	6	M 0.00000	1	2	Y	7	5	0	0	1	0	7	5
CONTROL	6	M 0.00000	2	3	Y	10	2	0	0	0	0	10	2
CONTROL	6	M 0.00000	2	4	Y	7	6	0	0	0	0	7	6
CONTROL	6	M 0.00000	3	5	Y	5	6	0	0	0	0	5	7
CONTROL	6	M 0.00000	3	6	Y	7	7	0	0	1	1	8	7
CONTROL	6	M 0.00000	4	7	Y	10	4	0	1	1	0	10	4
CONTROL	6	M 0.00000	4	8	Y	6	5	0	0	0	0	6	5
CONTROL	6	M 0.00000	5	9	Y	10	5	1	0	0	0	10	5
CONTROL	6	M 0.00000	5	10	Y	7	7	0	0	0	0	7	9
CONTROL	6	M 0.00000	6	11	Y	6	4	0	0	0	0	6	4
CONTROL	6	M 0.00000	6	12	Y	6	5	0	0	0	0	6	5
CONTROL	6	M 0.00000	7	13	Y	6	6	0	0	0	0	6	6
CONTROL	6	M 0.00000	7	14	Y	7	4	0	0	0	0	7	6
CONTROL	6	M 0.00000	8	15	Y	9	4	2	1	0	0	9	4
CONTROL	6	M 0.00000	8	16	Y	5	8	0	0	0	0	5	8
CONTROL	6	M 0.00000	9	17	Y	8	6	0	0	0	0	11	6
CONTROL	6	M 0.00000	9	18	Y	6	5	0	0	0	0	9	6
CONTROL	6	M 0.00000	10	19	Y	7	7	0	1	0	0	7	7
CONTROL	6	M 0.00000	10	20	Y	0	7	0	0	0	0	4	11

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"Manganese Sulfate"

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PHENO.	IMPLANTS L R	EARLY DEATHS		LATE DEATHS		CORPORA LUTEA L R	
							L	R	L	R	L	R
71-71	6	M 1.20000	91	181	Y	6 9	0	0	0	0	6	9
71-71	6	M 1.20000	91	182	YY	8 7	1	0	0	0	14	12
71-71	6	M 1.20000	92	183	N	0 0	0	0	0	0	0	0
71-71	6	M 1.20000	92	184	Y	6 6	0	0	0	0	6	6
71-71	6	M 1.20000	93	185	YY	8 6	0	1	0	0	9	6
71-71	6	M 1.20000	93	186	YY	4 6	0	0	0	0	6	8
71-71	6	M 1.20000	94	187	YY	9 4	0	0	0	0	9	4
71-71	6	M 1.20000	94	188	YY	3 6	0	0	0	0	3	7
71-71	6	M 1.20000	95	189	YY	10 4	1	0	0	0	10	5
71-71	6	M 1.20000	95	190	YY	3 6	0	1	0	0	4	8
71-71	6	M 1.20000	96	191	YY	5 10	0	0	0	0	5	10
71-71	6	M 1.20000	96	192	YY	7 4	1	0	0	0	7	6
71-71	6	M 1.20000	97	193	YY	8 7	0	0	0	0	9	7
71-71	6	M 1.20000	97	194	YY	6 5	0	0	0	0	7	5
71-71	6	M 1.20000	97	194	YY	3 11	0	0	0	1	3	11
71-71	6	M 1.20000	98	195	YY	12 4	0	0	0	0	12	6
71-71	6	M 1.20000	98	196	YY	6 6	0	0	0	0	7	6
71-71	6	M 1.20000	99	197	YY	6 7	1	0	0	0	6	7
71-71	6	M 1.20000	99	198	YY	5 8	0	0	0	1	6	9
71-71	6	M 1.20000	100	199	YY	0 0	0	0	0	0	6	0
71-71	6	M 1.20000	100	200	N	0 0	0	0	0	0	0	0

DOMINANT LETHAL STUDY OF COMPOUND 71-71

MANGANESE SULFATE

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	H	L	R	L	H
CONTROL	7	S	0.00000	1	1	Y	7	5	0	0	0	0	7	8
CONTROL	7	S	0.00000	1	2	Y	0	1	0	0	0	0	7	2
CONTROL	7	S	0.00000	2	3	Y	6	8	0	0	0	1	6	8
CONTROL	7	S	0.00000	2	4	Y	6	6	0	0	0	0	4	3
CONTROL	7	S	0.00000	3	5	Y	5	7	0	0	0	1	5	7
CONTROL	7	S	0.00000	3	6	Y	6	9	0	0	0	1	6	9
CONTROL	7	S	0.00000	4	7	Y	11	5	1	0	0	0	11	5
CONTROL	7	S	0.00000	4	8	Y	18	5	0	0	0	0	10	5
CONTROL	7	S	0.00000	5	9	Y	5	8	0	0	0	0	7	8
CONTROL	7	S	0.00000	5	10	Y	6	5	0	0	0	1	7	5
CONTROL	7	S	0.00000	6	11	Y	8	9	0	0	0	0	8	9
CONTROL	7	S	0.00000	6	12	Y	6	5	0	0	0	0	6	6
CONTROL	7	S	0.00000	7	13	Y	3	8	0	0	0	0	3	8
CONTROL	7	S	0.00000	7	14	Y	6	5	0	0	0	0	7	5
CONTROL	7	S	0.00000	8	15	Y	6	6	1	0	0	0	6	6
CONTROL	7	S	0.00000	8	16	Y	0	1	0	0	1	0	6	7
CONTROL	7	S	0.00000	9	17	Y	9	5	0	0	0	0	9	5
CONTROL	7	S	0.00000	9	18	Y	5	8	0	0	0	0	6	8
CONTROL	7	S	0.00000	10	19	Y	8	6	0	0	0	0	8	6
CONTROL	7	S	0.00000	10	20	Y								
71-71	7	S	.01200	81	161	Y	6	7	0	0	0	0	6	8
71-71	7	S	.01200	81	162	Y	8	5	0	0	0	1	9	5
71-71	7	S	.01200	82	163	Y	11	3	0	0	0	0	11	3
71-71	7	S	.01200	82	164	Y	7	6	0	0	0	0	7	6
71-71	7	S	.01200	83	165	Y	5	7	0	0	2	0	5	7
71-71	7	S	.01200	83	166	Y	7	7	0	0	0	0	7	7
71-71	7	S	.01200	84	167	Y	9	8	0	0	0	0	9	10
71-71	7	S	.01200	84	168	Y	9	5	1	0	0	0	9	5
71-71	7	S	.01200	85	169	Y	5	9	0	0	0	0	6	9
71-71	7	S	.01200	85	170	Y	9	5	1	0	0	0	9	4
71-71	7	S	.01200	86	171	Y	9	4	0	0	1	0	8	5
71-71	7	S	.01200	86	172	Y	8	4	0	0	0	0	12	8
71-71	7	S	.01200	87	173	Y	6	5	0	0	0	0	7	7
71-71	7	S	.01200	87	174	Y	6	7	0	0	1	0	6	6
71-71	7	S	.01200	88	175	Y	6	6	0	0	1	0	6	6
71-71	7	S	.01200	88	176	Y	0	2	0	0	0	0	8	4
71-71	7	S	.01200	89	177	Y	8	4	0	0	4	0	2	11
71-71	7	S	.01200	89	178	Y	2	11	0	0	0	0	9	5
71-71	7	S	.01200	90	179	Y	9	4	0	0	0	1	4	7
71-71	7	S	.01200	90	180	Y	4	7	0	0	1	0	0	

DOMINANT LETHAL STUDY OF COMPOUND 71-71

MANGANESE SULFATE

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	R	L	R	L	R
71-71	7	S	.12000	91	181	Y	7	6	1	0	2	1	7	6
71-71	7	S	.12000	91	182	Y	6	4	0	0	0	0	9	4
71-71	7	S	.12000	92	183	Y	7	4	0	0	0	0	8	4
71-71	7	S	.12000	92	184	Y	4	7	1	0	0	1	4	8
71-71	7	S	.12000	93	185	Y	4	9	0	0	0	0	7	9
71-71	7	S	.12000	93	186	Y	7	3	0	0	0	0	7	7
71-71	7	S	.12000	94	187	Y	7	6	0	0	0	0	10	2
71-71	7	S	.12000	94	188	Y	10	2	0	0	0	0	6	8
71-71	7	S	.12000	95	189	Y	6	8	0	0	1	0	3	8
71-71	7	S	.12000	95	190	Y	3	8	0	0	0	0	4	11
71-71	7	S	.12000	96	191	Y	4	11	0	1	0	0	9	3
71-71	7	S	.12000	96	192	Y	8	2	1	0	0	0	7	5
71-71	7	S	.12000	97	193	Y	7	4	1	0	0	0	8	8
71-71	7	S	.12000	97	194	Y	8	8	1	0	0	0	4	13
71-71	7	S	.12000	98	195	Y	4	12	0	0	0	0	8	6
71-71	7	S	.12000	98	196	Y	8	6	0	0	0	0	6	7
71-71	7	S	.12000	99	197	Y	0	1	0	0	0	0	10	1
71-71	7	S	.12000	99	198	Y	10	1	0	0	0	0	9	6
71-71	7	S	.12000	100	199	Y	9	6	1	0	0	0	9	5
71-71	7	S	.12000	100	200	Y	9	5	0	0	0	0	9	5
71-71	7	S	1.20000	101	201	Y	6	8	0	1	0	0	6	8
71-71	7	S	1.20000	101	202	Y	8	5	1	0	0	0	8	5
71-71	7	S	1.20000	102	203	Y	6	8	0	0	0	0	8	9
71-71	7	S	1.20000	102	204	Y	6	5	0	0	0	0	6	6
71-71	7	S	1.20000	103	205	Y	9	6	1	1	0	0	9	6
71-71	7	S	1.20000	103	206	Y	0	4	0	0	0	0	6	5
71-71	7	S	1.20000	103	207	Y	7	6	0	0	0	0	8	8
71-71	7	S	1.20000	104	208	Y	7	4	0	0	0	0	7	4
71-71	7	S	1.20000	104	209	Y	6	6	0	0	0	0	7	6
71-71	7	S	1.20000	105	210	Y	8	8	0	0	0	0	8	8
71-71	7	S	1.20000	105	211	Y	5	6	0	0	0	0	6	6
71-71	7	S	1.20000	106	212	Y	0	1	0	0	0	0	5	9
71-71	7	S	1.20000	106	213	Y	9	9	0	0	0	0	5	8
71-71	7	S	1.20000	107	214	Y	5	8	1	0	0	0	6	6
71-71	7	S	1.20000	107	215	Y	4	9	1	0	2	3	6	6
71-71	7	S	1.20000	108	216	Y	6	6	1	0	0	0	9	6
71-71	7	S	1.20000	108	217	Y	8	6	0	0	0	0	4	7
71-71	7	S	1.20000	109	218	Y	5	6	0	0	0	0	5	6
71-71	7	S	1.20000	109	219	Y	4	7	0	0	0	0	0	8
71-71	7	S	1.20000	110	220	Y	3	8	0	0	0	0	3	8

DOMINANT LETHAL STUDY OF COMPOUND 71-71

MANGANESE SULFATE

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TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	R	L	R	L	R
TEM	7	S	.00020	11	21	Y	10	5	0	1	0	0	10	5
TEM	7	S	.00020	11	22	Y	9	7	0	0	0	1	9	2
TEM	7	S	.00020	12	23	Y	4	9	0	1	0	0	4	9
TEM	7	S	.00020	12	24	Y	6	8	0	1	0	0	6	8
TEM	7	S	.00020	13	25	Y	6	5	0	0	0	0	6	7
TEM	7	S	.00020	13	26	Y	11	1	0	0	0	0	11	2
TEM	7	S	.00020	14	27	Y	7	9	0	0	0	0	8	9
TEM	7	S	.00020	14	28	Y	6	5	0	1	0	0	8	5
TEM	7	S	.00020	15	29	Y	6	8	0	0	0	0	6	8
TEM	7	S	.00020	15	30	Y	5	7	0	1	0	0	5	7
TEM	7	S	.00020	16	31	Y	5	8	0	0	0	0	5	8
TEM	7	S	.00020	16	32	Y	8	5	0	0	0	0	8	5
TEM	7	S	.00020	17	33	Y	9	7	0	0	1	0	9	7
TEM	7	S	.00020	17	34	Y	8	6	0	0	3	0	9	6
TEM	7	S	.00020	18	35	Y	8	4	0	0	0	0	9	4
TEM	7	S	.00020	18	36	Y	4	7	0	1	1	1	4	9
TEM	7	S	.00020	19	37	Y	7	7	1	0	0	0	7	7
TEM	7	S	.00020	19	38	Y	1	18	0	0	0	0	1	12
TEM	7	S	.00020	20	39	Y	5	7	0	0	0	0	7	8
TEM	7	S	.00020	20	40	Y	7	7	0	0	0	0	7	7
CONTROL	7	M	0.00000	1	1	Y	6	7	0	0	0	0	6	8
CONTROL	7	M	0.00000	1	2	Y	0	9	0	0	0	0	2	9
CONTROL	7	M	0.00000	2	3	Y	9	8	0	0	0	0	9	8
CONTROL	7	M	0.00000	2	4	Y	5	5	2	2	0	0	8	5
CONTROL	7	M	0.00000	3	5	Y	5	5	0	0	1	0	5	10
CONTROL	7	M	0.00000	3	6	Y	2	2	0	0	0	0	4	6
CONTROL	7	M	0.00000	4	7	Y	4	4	0	0	0	0	5	6
CONTROL	7	M	0.00000	4	8	Y	4	8	1	2	0	0	5	9
CONTROL	7	M	0.00000	5	9	Y	7	5	0	0	0	0	7	5
CONTROL	7	M	0.00000	5	10	Y	7	5	1	0	0	0	8	5
CONTROL	7	M	0.00000	6	11	Y	7	8	0	0	0	0	7	9
CONTROL	7	M	0.00000	6	12	Y	5	7	0	0	0	0	5	7
CONTROL	7	M	0.00000	7	13	Y	7	4	0	0	0	0	7	4
CONTROL	7	M	0.00000	7	14	Y	7	4	2	1	0	0	7	4
CONTROL	7	M	0.00000	8	15	Y	8	5	0	0	0	0	8	6
CONTROL	7	M	0.00000	8	16	Y	6	4	1	1	0	0	6	4
CONTROL	7	M	0.00000	9	17	Y	7	6	0	0	0	0	7	6
CONTROL	7	M	0.00000	9	18	Y	6	9	0	1	0	0	6	10
CONTROL	7	M	0.00000	10	19	Y	6	6	1	2	0	0	6	6
CONTROL	7	M	0.00000	10	20	Y	5	9	1	2	0	0	5	10

TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PHFG.	IMPLANTS	EARLY		LATE		CORPORA LUTEA		
								L	R	L	H	L	H	
71-71	7	M	.01200	71	141	Y	6	6	0	0	0	0	6	8
71-71	7	M	.01200	71	142	Y	5	9	0	0	0	0	5	9
71-71	7	M	.01200	72	143	Y	6	6	0	0	0	0	6	6
71-71	7	M	.01200	72	144	Y	3	9	0	0	0	0	3	9
71-71	7	M	.01200	73	145	Y	5	7	2	1	0	1	6	7
71-71	7	M	.01200	73	146	Y	6	6	0	0	0	0	6	6
71-71	7	M	.01200	74	147	Y	7	6	0	0	1	0	7	6
71-71	7	M	.01200	74	148	Y	6	3	0	0	0	0	6	3
71-71	7	M	.01200	76	151	Y	7	7	0	1	0	0	7	7
71-71	7	M	.01200	76	152	Y	6	6	0	0	0	0	6	7
71-71	7	M	.01200	77	153	Y	4	7	1	3	1	1	8	10
71-71	7	M	.01200	77	154	N	0	0	0	0	0	0	0	0
71-71	7	M	.01200	78	155	Y	6	7	0	0	0	0	6	7
71-71	7	M	.01200	78	156	Y	9	3	1	0	0	0	10	4
71-71	7	M	.01200	79	157	Y	6	7	2	0	0	1	7	7
71-71	7	M	.01200	79	158	Y	7	8	0	0	0	0	8	9
71-71	7	M	.01200	80	159	N	0	0	0	0	0	0	0	0
71-71	7	M	.01200	80	160	Y	6	6	0	0	0	0	6	6
71-71	7	M	.12000	81	161	Y	10	2	0	0	0	0	10	2
71-71	7	M	.12000	81	162	Y	6	7	0	0	0	0	6	8
71-71	7	M	.12000	82	163	Y	5	7	1	0	0	0	7	7
71-71	7	M	.12000	82	164	Y	5	9	0	0	0	0	5	9
71-71	7	M	.12000	83	165	Y	5	6	0	0	0	0	5	6
71-71	7	M	.12000	83	166	Y	7	5	0	0	0	0	10	6
71-71	7	M	.12000	84	167	Y	6	6	1	1	0	0	6	6
71-71	7	M	.12000	84	168	Y	6	8	0	0	0	0	6	8
71-71	7	M	.12000	85	169	Y	5	5	0	1	0	0	6	6
71-71	7	M	.12000	85	170	Y	6	7	1	0	0	0	7	7
71-71	7	M	.12000	86	171	Y	5	6	0	1	0	0	5	7
71-71	7	M	.12000	86	172	Y	8	4	1	0	0	0	8	4
71-71	7	M	.12000	87	173	Y	3	9	0	0	0	1	3	13
71-71	7	M	.12000	87	174	Y	9	4	0	0	0	0	11	4
71-71	7	M	.12000	88	175	Y	10	2	0	0	0	0	10	2
71-71	7	M	.12000	88	176	Y	5	5	0	0	0	1	6	5
71-71	7	M	.12000	89	177	Y	4	6	0	0	0	1	4	7
71-71	7	M	.12000	89	178	Y	7	4	0	0	0	0	8	4
71-71	7	M	.12000	90	179	Y	6	6	0	0	0	0	6	6
71-71	7	M	.12000	90	180	Y	6	6	0	0	0	0	6	6

DOMINANT LETHAL STUDY OF COMPOUND 71-71

MANGANESE SULFATE

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORAL LUTEA	
						L	K	L	R	L	R	L	R
71-71	7	M 1.20000	91	181	Y	1	7	0	0	0	0	1	8
71-71	7	M 1.20000	91	182	YY	5	6	0	0	0	0	6	6
71-71	7	M 1.20000	92	183	YY	2	7	0	0	0	1	8	7
71-71	7	M 1.20000	92	184	YY	6	6	0	0	0	0	6	7
71-71	7	M 1.20000	93	185	YY	8	4	0	0	0	0	13	5
71-71	7	M 1.20000	93	186	YY	0	7	0	0	0	1	6	7
71-71	7	M 1.20000	94	187	YY	6	7	0	0	0	0	6	7
71-71	7	M 1.20000	94	188	YY	9	3	0	0	0	0	7	9
71-71	7	M 1.20000	95	189	YY	7	9	0	0	0	0	7	9
71-71	7	M 1.20000	95	190	YY	4	8	0	0	1	2	4	8
71-71	7	M 1.20000	96	191	YY	4	8	0	0	0	0	6	7
71-71	7	M 1.20000	96	192	YY	5	7	0	0	0	0	5	8
71-71	7	M 1.20000	97	193	YY	5	8	0	0	0	0	6	8
71-71	7	M 1.20000	97	194	YY	6	8	0	0	0	0	11	4
71-71	7	M 1.20000	98	195	YY	10	4	0	0	0	0	8	5
71-71	7	M 1.20000	98	196	YY	8	5	0	0	0	0	8	4
71-71	7	M 1.20000	99	197	YY	8	4	0	0	0	0	7	4
71-71	7	M 1.20000	99	198	YY	7	4	0	0	0	0	13	7
71-71	7	M 1.20000	100	199	YY	8	4	0	0	0	0	9	6
71-71	7	M 1.20000	100	200	Y	9	5	0	0	0	0	0	0

DOMINANT LETHAL STUDY OF COMPOUND 71-71

MANGANESE SULFATE

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TEST MATERIAL	WEEK	S/M DOSE	MALE NO.	FEMALE NO.	PRFG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
						L	R	L	R	L	R	L	R
CONTROL	8	S 0.00000	1	1	Y	4	6	0	0	0	0	5	6
CONTROL	8	S 0.00000	1	2	Y	6	8	0	4	0	0	6	8
CONTROL	8	S 0.00000	2	3	Y	8	2	0	0	0	0	8	4
CONTROL	8	S 0.00000	2	4	Y	9	3	0	0	1	0	9	3
CONTROL	8	S 0.00000	3	5	Y	6	7	0	0	0	0	6	8
CONTROL	8	S 0.00000	3	6	Y	6	7	0	0	0	0	6	7
CONTROL	8	S 0.00000	4	7	Y	5	8	0	2	0	0	4	9
CONTROL	8	S 0.00000	4	8	Y	4	9	0	1	0	0	4	9
CONTROL	8	S 0.00000	5	9	Y	7	6	1	3	0	0	7	6
CONTROL	8	S 0.00000	5	10	Y	11	2	2	0	0	0	12	2
CONTROL	8	S 0.00000	6	11	Y	4	7	0	0	0	0	4	7
CONTROL	8	S 0.00000	6	12	Y	6	5	0	0	0	0	6	6
CONTROL	8	S 0.00000	7	13	Y	10	1	0	0	0	0	10	2
CONTROL	8	S 0.00000	7	14	Y	3	10	0	0	0	0	3	10
CONTROL	8	S 0.00000	8	15	Y	6	8	0	0	0	1	6	8
CONTROL	8	S 0.00000	8	16	Y	5	7	0	0	0	0	6	8
CONTROL	8	S 0.00000	9	17	Y	8	7	1	0	0	0	8	7
CONTROL	8	S 0.00000	9	18	Y	7	7	1	0	0	0	7	7
CONTROL	8	S 0.00000	10	19	Y	3	7	0	0	0	0	3	7
CONTROL	8	S 0.00000	10	20	Y	8	5	4	2	0	0	8	5
71-71	8	S .01200	81	161	Y	3	11	0	1	0	0	3	11
71-71	8	S .01200	81	162	Y	6	6	1	0	0	0	6	7
71-71	8	S .01200	82	163	Y	8	6	0	0	0	0	8	6
71-71	8	S .01200	82	164	Y	9	6	0	0	0	0	10	6
71-71	8	S .01200	83	165	Y	4	7	0	0	0	0	7	7
71-71	8	S .01200	83	166	Y	7	6	0	0	1	0	7	7
71-71	8	S .01200	84	167	Y	9	5	0	0	0	0	9	5
71-71	8	S .01200	84	168	Y	8	4	2	0	0	0	8	4
71-71	8	S .01200	85	169	Y	10	3	2	0	1	0	10	3
71-71	8	S .01200	85	170	Y	9	4	2	1	0	0	9	4
71-71	8	S .01200	86	171	Y	6	3	0	0	0	0	6	4
71-71	8	S .01200	86	172	Y	3	8	0	0	0	0	4	9
71-71	8	S .01200	87	173	Y	6	6	0	0	2	3	6	8
71-71	8	S .01200	87	174	Y	5	9	0	0	0	0	5	9
71-71	8	S .01200	88	175	Y	7	6	0	0	0	0	7	6
71-71	8	S .01200	88	176	Y	4	8	0	0	0	0	4	8
71-71	8	S .01200	89	177	Y	8	6	0	0	0	1	9	6
71-71	8	S .01200	89	178	Y	5	7	1	0	0	0	5	7
71-71	8	S .01200	90	179	Y	7	5	0	0	0	0	7	6
71-71	8	S .01200	90	180	Y	11	6	0	0	0	0	11	6

DOMINANT LETHAL STUDY OF COMPOUND 71-71

CHINESE SULFATE

PAGE 37

TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PREG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CONPLURA LUTEA	
							L	R	L	R	L	R	L	R
71-71	8	S	.12000	91	181	Y	3	0	0	0	0	0	9	5
71-71	8	S	.12000	91	182	Y	7	7	0	0	0	0	7	7
71-71	8	S	.12000	92	183	Y	3	8	0	0	0	0	4	8
71-71	8	S	.12000	92	184	Y	9	5	1	0	0	0	9	5
71-71	8	S	.12000	93	185	Y	9	4	0	0	0	0	9	4
71-71	8	S	.12000	93	186	Y	10	4	2	0	0	0	10	4
71-71	8	S	.12000	94	187	Y	7	8	0	0	0	0	7	8
71-71	8	S	.12000	94	188	Y	5	6	0	0	0	0	5	6
71-71	8	S	.12000	95	189	Y	4	8	0	1	0	0	10	8
71-71	8	S	.12000	95	190	Y	8	3	5	2	0	0	8	3
71-71	8	S	.12000	96	191	Y	4	9	0	1	0	0	4	9
71-71	8	S	.12000	96	192	Y	6	6	0	0	0	0	7	6
71-71	8	S	.12000	97	193	Y	6	7	0	1	0	0	6	7
71-71	8	S	.12000	97	194	Y	10	5	0	1	0	0	10	5
71-71	8	S	.12000	98	195	Y	6	7	0	2	0	0	6	7
71-71	8	S	.12000	98	196	Y	5	8	0	0	0	0	5	8
71-71	8	S	.12000	99	197	Y	6	5	0	1	0	0	7	5
71-71	8	S	.12000	99	198	Y	7	8	0	0	0	0	7	8
71-71	8	S	.12000	100	199	Y	7	8	0	0	0	0	7	8
71-71	8	S	.12000	100	200	Y	3	0	0	0	0	0	8	3
71-71	8	S	1.20000	101	201	Y	8	7	0	0	0	0	8	7
71-71	8	S	1.20000	101	202	Y	4	9	0	0	0	0	4	10
71-71	8	S	1.20000	102	203	Y	8	5	0	0	0	0	9	7
71-71	8	S	1.20000	102	204	Y	3	11	1	1	0	0	3	11
71-71	8	S	1.20000	103	205	Y	4	10	0	0	0	0	4	11
71-71	8	S	1.20000	103	206	Y	3	6	0	0	0	0	4	6
71-71	8	S	1.20000	104	207	Y	5	9	1	1	0	0	6	9
71-71	8	S	1.20000	104	208	Y	8	7	1	1	0	0	9	8
71-71	8	S	1.20000	105	209	Y	7	3	1	1	0	0	3	9
71-71	8	S	1.20000	105	210	Y	3	7	0	0	0	0	9	5
71-71	8	S	1.20000	106	211	Y	8	5	0	0	0	0	7	6
71-71	8	S	1.20000	106	212	Y	7	5	1	0	0	0	4	10
71-71	8	S	1.20000	107	213	Y	4	10	0	0	0	0	7	7
71-71	8	S	1.20000	107	214	Y	7	7	1	0	0	0	5	8
71-71	8	S	1.20000	108	215	Y	5	8	0	0	0	0	4	6
71-71	8	S	1.20000	108	216	Y	3	5	0	0	1	0	9	5
71-71	8	S	1.20000	109	217	Y	9	3	0	0	1	0	7	7
71-71	8	S	1.20000	109	218	Y	7	7	0	0	0	0	7	3
71-71	8	S	1.20000	110	219	Y	9	3	0	0	1	0	7	6
71-71	8	S	1.20000	110	220	Y	7	4	0	0	1	1	0	0

DOMINANT LETHAL STUDY OF COMPOUND 71-77

MANGANESE SULFATE

PAGE 3H

TEST MATERIAL	WEEK	S/M	DOSE	MALE NO.	FEMALE NO.	PRFG.	IMPLANTS		EARLY DEATHS		LATE DEATHS		CORPORA LUTEA	
							L	R	L	H	L	H	L	H
TEM	8	S	.00020	11	21	Y	6	10	0	0	0	0	8	10
TEM	8	S	.00020	11	22	Y	9	5	0	1	1	0	9	7
TEM	8	S	.00020	12	23	Y	4	9	1	1	0	0	6	9
TEM	8	S	.00020	12	24	Y	4	5	2	0	0	3	6	5
TEM	8	S	.00020	13	25	Y	6	5	0	0	1	1	6	5
TEM	8	S	.00020	13	26	Y	4	9	1	0	0	0	4	9
TEM	8	S	.00020	14	27	Y	9	5	0	0	0	0	9	6
TEM	8	S	.00020	14	28	Y	7	4	0	0	0	0	7	4
TEM	8	S	.00020	15	29	Y	6	4	0	0	0	0	6	4
TEM	8	S	.00020	15	30	Y	7	6	0	1	0	0	7	6
TEM	8	S	.00020	16	31	Y	8	3	0	0	0	0	8	4
TEM	8	S	.00020	16	32	Y	5	8	0	0	0	0	6	9
TEM	8	S	.00020	17	33	Y	7	3	0	0	0	1	7	4
TEM	8	S	.00020	17	34	Y	6	7	0	0	0	0	6	7
TEM	8	S	.00020	18	35	Y	5	8	0	0	0	0	5	8
TEM	8	S	.00020	18	36	Y	3	8	0	0	0	0	3	9
TEM	8	S	.00020	19	37	Y	8	5	0	1	0	0	8	6
TEM	8	S	.00020	19	38	Y	5	9	1	0	0	0	8	13
TEM	8	S	.00020	20	39	Y	6	5	2	0	0	0	8	5
TEM	8	S	.00020	20	40	Y	9	3	0	0	0	0	9	3

ARMITAGE TEST FOR A LINEAR TREND IN PROPORTIONS FOR THE FERTILITY INDEX
 (1 DEGREE OF FREEDOM)
 BASED ON THE DOSE LEVELS

WEEK	12 MG/KG		120 MG/KG		1200 MG/KG		CHISQ (C-1)	CHISQ (1)	ARMTG CHISQ
	N PRG	N MTD	N PRG	N MTD	N PRG	N MTD			
	---	---	---	---	---	---			
SINGLE TREATMENT									
1	20	20	16	20	19	20	5.67	.22	5.45
2	19	20	16	20	20	20	5.67	2.26	3.41
3	20	20	18	20	20	20	4.14	.75	3.38
4	20	20	20	20	20	20	0.00	0.00	0.00
5	20	20	20	20	19	20	2.03	2.02	.01
6	20	20	20	20	20	20	0.00	0.00	0.00
7	20	20	20	20	20	20	0.00	0.00	0.00
8	20	20	20	20	20	20	0.00	0.00	0.00
MULTIPLE TREATMENT									
1	18	20	16	20	17	20	.78	.01	.78
2	17	18	19	20	20	20	1.10	1.10	.00
3	17	18	20	20	20	20	2.26	.70	1.56
4	18	18	20	20	19	20	1.93	1.92	.01
5	18	18	20	20	20	20	0.00	0.00	0.00
6	17	18	19	20	18	20	.46	.45	.01
7	16	18	20	20	20	20	4.60	1.42	3.18

ARMITAGE TEST FOR A LINEAR TREND IN PROPORTIONS FOR THE FERTILITY INDEX
 (1 DEGREE OF FREEDOM) BASED ON THE LOGARITHMS OF THE DOSE LEVELS

WEEK	12 MG/KG		120 MG/KG		1200 MG/KG		CHISQ (C-1)	CHISQ (1)	ARMTG CHISQ
	N	N	N	N	N	PRG MTD			
	PRG	MTD	PRG	MTD	PRG	MTD			
SINGLE TREATMENT									
1	20	20	16	20	19	20	5.67	.33	5.35
2	19	20	16	20	20	20	5.67	.33	5.35
3	20	20	18	20	20	20	4.14	.00	4.14
4	20	20	20	20	20	20	0.00	0.00	0.00
5	20	20	20	20	19	20	2.03	1.53	.51
6	20	20	20	20	20	20	0.00	0.00	0.00
7	20	20	20	20	20	20	0.00	0.00	0.00
8	20	20	20	20	20	20	0.00	0.00	0.00
MULTIPLE TREATMENT									
1	18	20	16	20	17	20	.78	.20	.59
2	17	18	19	20	20	20	1.10	.90	.19
3	17	18	20	20	20	20	2.26	1.67	.60
4	18	18	20	20	19	20	1.93	1.45	.48
5	18	18	20	20	20	20	0.00	0.00	0.00
6	17	18	19	20	18	20	.46	.31	.16
7	16	18	20	20	20	20	4.60	3.39	1.21

ARMITAGE TEST FOR A LINEAR TREND IN PROPORTIONS FOR THE FERTILITY INDEX
(2 DEGREES OF FREEDOM)
BASED ON THE DOSE LEVELS AND INCLUDING THE CONTROL GROUP

WEEK	CONTROL		12 MG/KG		120 MG/KG		1200 MG/KG		CHISQ (C-1)	CHISQ (1)	ARMTG CHISQ
	N	N	N	N	N	N	PRG	MTD			
	PHG	MTD	PRG	MTD	PRG	MTD	PRG	MTD			
SINGLE TREATMENT											
1	15	20	20	20	16	20	19	20	7.77	1.23	6.54
2	20	20	19	20	16	20	20	20	9.17	1.16	8.01
3	20	20	20	20	18	20	20	20	6.15	.37	5.79
4	20	20	20	20	20	20	20	20	0.00	0.00	0.00
5	20	20	20	20	20	20	19	20	3.04	3.01	.03
6	20	20	20	20	20	20	20	20	0.00	0.00	0.00
7	20	20	20	20	20	20	20	20	0.00	0.00	0.00
8	20	20	20	20	20	20	20	20	0.00	0.00	0.00
MULTIPLE TREATMENT											
1	20	20	18	20	16	20	17	20	4.38	.61	3.77
2	20	20	17	18	19	20	20	20	2.17	.61	1.57
3	20	20	17	18	20	20	20	20	3.38	.43	2.95
4	20	20	18	18	20	20	19	20	2.94	2.91	.03
5	18	20	18	18	20	20	20	20	5.95	.93	5.02
6	20	20	17	18	19	20	18	20	2.06	1.40	.66
7	20	20	16	18	20	20	20	20	6.84	.87	5.97

T-TEST OF THE NUMBER OF IMPLANTATIONS IN PREGNANT FEMALES

WEEK	CONTROL				71-71 12 MG/KG				71-71 120 MG/KG				71-71 1200 MG/KG				TEM		.2 MG/KG					
	N PRG	MEAN	STD DEV	PRG	N PRG	MEAN	STD DEV	DF	T	N PRG	MEAN	STD DEV	DF	T	N PRG	MEAN	STD DEV	DF	T	N PRG	MEAN	STD DEV	DF	T
SINGLE TREATMENT																								
1	15	11.80	3.51	20	11.60	2.74	33	.189	16	11.00	3.27	29	.657	19	11.95	1.43	32	.167	17	11.82	1.51	30	.025	
2	20	10.70	2.08	19	11.32	1.38	37	1.084	16	10.94	2.21	34	.331	20	11.60	1.90	38	1.428	20	10.10	2.05	38	.919	
3	20	12.25	1.71	20	12.30	1.56	38	.097	18	11.11	2.14	36	1.820	20	11.25	1.65	38	1.880	20	7.35	3.20	38	6.038	
4	20	11.85	2.54	20	12.05	1.73	38	.291	20	13.05	2.28	38	1.572	20	12.15	1.81	38	.430	17	6.06	3.33	35	6.001	
5	20	12.30	3.42	20	12.55	1.79	38	.290	20	12.45	3.65	38	.134	19	12.00	1.83	37	.339	20	11.30	2.43	38	1.066	
6	20	11.50	1.93	20	11.45	3.19	38	.060	20	11.45	1.28	38	.097	20	11.95	3.46	38	.508	20	12.65	1.63	38	2.033	
7	20	11.30	4.49	20	12.50	2.80	38	1.015	20	12.05	3.27	38	.604	20	11.90	3.75	38	.459	20	13.05	1.57	38	1.647	
8	20	12.45	1.39	20	12.85	1.69	38	.815	20	12.05	3.39	38	.487	20	12.60	2.01	38	.274	20	12.35	1.69	38	.204	
MULTIPLE TREATMENT																								
1	20	11.15	2.68	18	11.06	2.86	36	.105	16	11.00	3.12	34	.155	17	12.29	1.83	35	1.488						
2	20	12.45	1.50	17	11.41	1.70	35	1.973	19	11.79	2.02	37	1.164	20	12.95	1.54	38	1.040						
3	20	11.75	2.88	17	12.47	1.94	35	.875	20	11.95	2.65	38	.229	20	11.80	2.57	38	.058						
4	20	12.40	4.33	18	12.44	3.40	36	.035	20	12.35	3.13	38	.042	19	13.11	1.24	37	.683						
5	18	11.89	4.44	18	11.17	3.54	34	.540	20	11.35	2.52	36	.466	20	12.75	1.83	36	.796						
6	20	12.20	1.85	17	13.53	1.55	35	2.344	19	13.16	2.59	37	1.335	18	12.83	2.15	36	.976						
7	20	11.85	3.05	16	12.37	1.36	34	.639	20	11.90	1.17	38	.069	20	11.95	2.09	38	.121						

REGRESSION FITS OF THE NUMBER, U, OF IMPLANTATIONS ON 1) DOSE AND 2) LOG DOSE
(PREDICTED U = A + B*x)
CONTROL GROUP EXCLUDED

WEEK	X	N	XBAR	SD X	UBAR	SD U	B	A	TB	DF	VARU X	Cv U	VARB	VARA	VARUBAR
SINGLE TREATMENT															
1	DOSE	55	.45	.55	11.55	2.54	.500	11.319	.792	53	6.4825	.2205	.3985	.1999	.1179
	LOG DOSE	55	-2.16	1.96	11.55	2.54	.073	11.703	.410	53	6.5384	.2215	.0316	.2668	.1189
2	DOSE	55	.48	.55	11.31	1.82	.378	11.130	.841	53	3.3467	.1618	.2016	.1064	.0608
	LOG DOSE	55	-2.08	1.96	11.31	1.82	.063	11.441	.496	53	3.3757	.1625	.0163	.1319	.0614
3	DOSE	58	.46	.55	11.57	1.84	-.497	11.795	-.119	56	3.3574	.1584	.1970	.0987	.0579
	LOG DOSE	58	-2.12	1.93	11.57	1.84	-.228	11.086	-.846	56	3.2357	.1555	.0153	.1244	.0558
4	DOSE	60	.44	.54	12.42	1.98	-.288	12.544	-.602	58	3.9509	.1601	.2289	.1110	.0658
	LOG DOSE	60	-2.12	1.90	12.42	1.98	.022	12.463	.159	58	3.9739	.1605	.0187	.1505	.0662
5	DOSE	59	.43	.54	12.34	2.55	-.444	12.531	-.709	57	6.5601	.2076	.3933	.1843	.1112
	LOG DOSE	59	-2.16	1.89	12.34	2.55	-.119	12.083	-.666	57	6.5668	.2077	.0318	.2594	.1113
6	DOSE	60	.44	.54	11.62	2.77	.438	11.422	.653	58	7.7737	.2400	.4503	.2163	.1296
	LOG DOSE	60	-2.12	1.90	11.62	2.77	.109	11.847	.567	58	7.7876	.2402	.0367	.2949	.1298
7	DOSE	60	.44	.54	12.15	3.25	-.357	12.308	-.453	58	10.7147	.2694	.6207	.3009	.1786
	LOG DOSE	60	-2.12	1.90	12.15	3.25	-.130	11.874	-.580	58	10.6905	.2691	.0504	.4048	.1782
8	DOSE	60	.44	.54	12.50	2.46	-.081	12.464	-.136	58	6.1532	.1984	.3564	.1728	.1026
	LOG DOSE	60	-2.12	1.90	12.50	2.46	-.054	12.385	-.319	58	6.1444	.1983	.0290	.2327	.1024
MULTIPLE TREATMENTS															
1	DOSE	51	.44	.54	11.45	2.67	1.101	10.964	1.609	49	6.9129	.2296	.4685	.2270	.1355
	LOG DOSE	51	-2.17	1.93	11.45	2.67	.266	12.028	1.370	49	7.0097	.2312	.0378	.3147	.1374
2	DOSE	56	.47	.55	12.09	1.85	1.198	11.523	2.791	54	3.0515	.1445	.1844	.0957	.0545
	LOG DOSE	56	-2.00	1.88	12.09	1.85	.339	12.766	2.699	54	3.0767	.1451	.0158	.1178	.0549
3	DOSE	57	.47	.55	12.05	2.40	-.373	12.227	-.631	55	5.8276	.2003	.3495	.1784	.1022
	LOG DOSE	57	-2.00	1.87	12.05	2.40	-.143	11.766	-.832	55	5.7969	.1998	.0297	.2203	.1017
4	DOSE	57	.45	.54	12.63	2.73	.618	12.356	.913	55	7.4733	.2164	.4580	.2222	.1311
	LOG DOSE	57	-2.08	1.87	12.63	2.73	.145	12.934	.742	55	7.5114	.2170	.0383	.2975	.1318
5	DOSE	58	.46	.54	11.78	2.73	1.317	11.172	2.032	56	7.0860	.2261	.4199	.2106	.1222
	LOG DOSE	58	-2.04	1.88	11.78	2.73	.349	12.487	1.846	56	7.1722	.2274	.0357	.2722	.1237
6	DOSE	54	.45	.54	13.17	2.13	-.462	13.373	-.849	52	4.5807	.1626	.2964	.1438	.0848
	LOG DOSE	54	-2.08	1.87	13.17	2.13	-.151	12.853	-.963	52	4.5629	.1622	.0246	.1907	.0845
7	DOSE	56	.47	.55	12.05	1.59	-.170	12.134	-.430	54	2.5623	.1328	.1556	.0809	.0458
	LOG DOSE	56	-1.96	1.86	12.05	1.59	-.088	11.882	-.757	54	2.5441	.1323	.0134	.0968	.0454

REGRESSION FITS OF THE NUMBER, U, OF IMPLANTATIONS ON DOSE
(PREDICTED U = A + B*X)

CONTROL GROUP INCLUDED

WEEK	X	N	XBAR	SD X	UBAR	SD U	B	A	TB	DF	VARU X	CV U	VARB	VARA	VARUBAR
SINGLE TREATMENT															
1	DOSE	70	.36	.52	11.60	2.75	.362	11.471	.567	68	7.6228	.2380	.4078	.1607	.1089
2	DOSE	75	.35	.52	11.15	1.90	.528	10.963	1.244	73	3.5868	.1699	.1801	.0697	.0478
3	DOSE	76	.34	.51	11.74	1.82	-.650	11.964	-1.619	76	3.2417	.1533	.1611	.0600	.0416
4	DOSE	80	.33	.51	12.27	2.13	-.059	12.295	-.124	78	4.5882	.1745	.2269	.0825	.0574
5	DOSE	79	.32	.50	12.33	2.77	-.368	12.448	-.583	77	7.7508	.2258	.3983	.1394	.0981
6	DOSE	80	.33	.51	11.59	2.58	.412	11.450	.717	78	6.6917	.2232	.3309	.1203	.0836
7	DOSE	80	.33	.51	11.94	3.59	-.024	11.946	-.030	78	13.0343	.3024	.6446	.2344	.1629
8	DOSE	80	.33	.51	12.49	2.23	.086	12.459	.172	78	5.0492	.1799	.2497	.0908	.0631
MULTIPLE TREATMENTS															
1	DOSE	71	.32	.50	11.37	2.66	1.034	11.038	1.650	69	6.8942	.2310	.3926	.1367	.0971
2	DOSE	76	.35	.51	12.18	1.76	.873	11.880	2.264	74	2.9501	.1410	.1486	.0569	.0388
3	DOSE	77	.35	.51	11.97	2.52	-.208	12.046	-.366	75	6.4145	.2115	.3224	.1218	.0833
4	DOSE	77	.33	.50	12.57	3.19	.603	12.372	.827	75	10.2381	.2545	.5315	.1909	.1330
5	DOSE	76	.35	.51	11.80	3.19	1.088	11.422	1.531	74	9.9815	.2677	.5049	.1933	.1313
6	DOSE	74	.33	.50	12.91	2.09	-.047	12.921	-.094	72	4.4486	.1634	.2423	.0858	.0601
7	DOSE	76	.35	.51	12.00	2.05	-.069	12.024	-.149	74	4.2690	.1722	.2158	.0826	.0562

T-TEST OF THE (TRANSFORMED) PRE-IMPLANTATION LOSSES IN PREGNANT FEMALES
(LOSSES TAKEN AS A SUBSET OF CORPORA LUTEA)

T-TEST OF THE NUMBER OF DEAD IMPLANTS

WEEK	CONTROL				71-71 12 MG/KG				71-71 120 MG/KG				71-71 1200 MG/KG				TEM		.2 MG/KG				
	N	PRG	MEAN	STD DEV	N	PRG	MEAN	STD DEV	DF	T	N	PRG	MEAN	STD DEV	DF	T	N	PRG	MEAN	STD DEV	DF	T	
SINGLE TREATMENT																							
1	15	.40	.83	20	.35	.49	33	.224	16	.94	1.12	29	1.508	19	.53	1.12	32	.364	17	3.24	2.63	30	3.991
2	20	.40	.75	19	.74	1.05	37	1.158	16	.63	.89	34	.824	20	.65	.93	38	.932	20	6.65	4.16	38	6.575
3	20	.80	1.47	20	.80	1.01	38	0.000	18	.78	1.26	36	.050	20	.35	.59	38	1.269	20	5.95	3.28	38	6.399
4	20	.45	.60	20	1.05	1.28	38	1.900	20	.85	1.23	38	1.309	20	.80	1.58	38	.927	17	5.41	2.74	35	7.894
5	20	1.20	1.44	20	1.10	1.62	38	.207	20	.65	.75	38	1.520	19	1.37	1.74	37	.330	20	3.00	2.08	38	3.187
6	20	.75	.85	20	.55	1.19	38	.611	20	.35	.59	38	1.731	20	.55	.94	38	.704	20	.35	.67	38	1.651
7	20	.35	.49	20	.60	.99	38	1.009	20	.65	1.04	38	1.167	20	.70	1.49	38	.998	20	.70	.92	38	1.498
8	20	1.15	1.69	20	.90	1.37	38	.513	20	.85	1.60	38	.576	20	.60	.75	38	1.326	20	.90	1.25	38	.531
MULTIPLE TREATMENT																							
1	20	1.75	1.77	18	.89	1.32	36	1.681	16	.81	1.17	34	1.820	17	.59	.87	35	2.458					
2	20	1.10	1.25	17	1.24	1.92	35	.257	19	.58	.84	37	1.519	20	1.00	1.65	38	.216					
3	20	.90	1.41	17	1.65	1.84	35	1.399	20	1.30	2.03	38	.724	20	.30	.47	38	1.805					
4	20	1.45	1.76	18	1.67	3.09	36	.269	20	.80	1.06	38	1.415	19	.68	1.00	37	1.656					
5	18	.83	1.47	18	1.44	2.50	34	.894	20	1.10	1.83	36	.492	20	1.00	1.30	36	.372					
6	20	.50	.89	17	.47	.94	35	.098	19	.68	.89	37	.648	18	.44	.51	36	.233					
7	20	1.05	1.36	16	1.00	1.79	34	.095	20	.55	.60	38	1.506	20	.25	.72	38	2.333					

ARMITAGE TEST FOR A LINEAR TREND IN PROPORTIONS FOR THE DEATH INDEX
(1 DEGREE OF FREEDOM)
BASED ON THE DOSE LEVELS

WEEK	12 MG/KG		120 MG/KG		1200 MG/KG		CHISQ (C-1)	CHISQ (1)	ARMTG CHISQ
	N	N	N	N	N	N			
	WDT	PRG	WDI	PRG	WDI	PRG			
SINGLE TREATMENT									
1	7	20	8	16	4	19	3.22	2.10	1.12
2	8	19	7	16	9	20	.03	.03	.01
3	10	20	8	18	6	20	1.75	1.69	.06
4	12	20	10	20	7	20	2.54	2.28	.26
5	9	20	10	20	12	19	1.37	1.32	.05
6	6	20	6	20	6	20	-.00	0.00	-.00
7	8	20	8	20	6	20	.57	.57	.00
8	9	20	9	20	9	20	-.00	0.00	-.00
MULTIPLE TREATMENT									
1	8	18	7	16	7	17	.04	.04	.00
2	7	17	8	19	9	20	.06	.06	.00
3	12	17	14	20	6	20	8.55	8.51	.04
4	11	18	10	20	9	19	.79	.38	.40
5	10	18	10	20	11	20	.15	.02	.13
6	4	17	9	19	8	18	2.50	.51	1.99
7	6	16	10	20	3	20	5.59	4.67	.92

ARMITAGE TEST FOR A LINEAR TREND IN PROPORTIONS FOR THE DEATH INDEX
 (1 DEGREE OF FREEDOM) BASED ON THE LOGARITHMS OF THE DOSE LEVELS

WEEK	12 MG/KG		120 MG/KG		1200 MG/KG		CHISQ (C-1)	CHISQ (1)	ARMTG CHISQ
	N	WDI	N	WDI	N	WDI			
	PRG		PRG		PRG				
SINGLE TREATMENT									
1	7	20	8	16	4	19	3.22	.80	2.42
2	8	10	7	16	9	20	.03	.03	.00
3	10	20	8	18	6	20	1.75	1.65	.10
4	12	20	10	20	7	20	2.54	2.50	.03
5	9	20	10	20	12	19	1.37	1.28	.09
6	6	20	6	20	6	20	-.00	0.00	-.00
7	8	20	8	20	6	20	.57	.43	.14
8	9	20	9	20	9	20	-.00	0.00	-.00
MULTIPLE TREATMENT									
1	8	18	7	16	7	17	.04	.04	.00
2	7	17	8	19	9	20	.06	.06	.00
3	12	17	14	20	6	20	8.55	6.51	2.04
4	11	18	10	20	9	19	.79	.69	.09
5	10	18	10	20	11	20	.15	.00	.15
6	4	17	9	19	8	18	2.56	1.57	.93
7	6	16	10	20	3	20	5.59	2.37	3.22

ARMITAGE TEST FOR A LINEAR TREND IN POPULATIONS FOR THE DEATH INDEX
(2 DEGREES OF FREEDOM) BASED ON THE DOSE LEVELS AND INCLUDING THE CONTROL GROUP

WEEK	CONTROL		12 MG/KG		120 MG/KG		1200 MG/KG		CHISQ (C-1)	CHISQ (1)	ARMTG CHISQ		
	N	N	N	N	WDI	PRG	WDI	PRG				WDI	PRG
	WDI	PRG	WDI	PRG	WDI	PRG	WDI	PRG				WDI	PRG

SINGLE TREATMENT

1	4	15	7	20	8	16	4	19	3.63	1.35	2.29
2	5	20	8	19	7	16	9	20	2.18	.56	1.62
3	7	20	10	20	8	18	6	20	2.03	1.02	1.01
4	8	20	12	20	10	20	7	20	2.97	1.32	1.65
5	11	20	9	20	10	20	12	19	1.40	.98	.42
6	11	20	6	20	6	20	6	20	4.06	.59	3.46
7	7	20	8	20	8	20	6	20	.59	.42	.17
8	10	20	9	20	9	20	9	20	.15	.02	.13

MULTIPLE TREATMENT

1	15	20	8	18	7	16	7	17	5.49	1.32	4.56
2	13	20	7	17	8	19	9	20	2.95	.22	2.73
3	8	20	12	17	14	20	6	20	9.98	4.63	5.35
4	12	20	11	18	10	20	9	19	1.11	.63	.49
5	8	18	10	18	10	20	11	20	.59	.15	.44
6	6	20	4	17	9	19	8	18	3.06	.89	2.17
7	9	20	6	16	10	20	3	20	6.16	5.27	.90

PROBIT ANALYSIS OF THE PROPORTION OF PREGNANT FEMALES WITH ONE OR MORE DEAD IMPLANTS
PROBIT = A + B(LOG DOSE)

WEEK	B	A	CHISQ	DF
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SINGLE TREATMENT

1	-.190	4.418	2.51	1
2	.037	4.873	.00	1
3	-.260	4.537	.12	1
4	-.319	4.663	.04	1
5	.229	5.280	.09	1
6	-.000	4.476	.00	1
7	-.134	4.534	.15	1
8	-.000	4.874	.00	1

MULTIPLE TREATMENT

1	-.041	4.788	.00	1
2	.049	4.863	.00	1
3	-.553	4.687	1.98	1
4	-.173	4.911	.10	1
5	-.005	5.082	.15	1
6	.276	4.959	1.01	1
7	-.348	4.272	3.53	1

T-TEST OF THE (TRANSFORMED) NUMBER OF DEAD IMPLANTS
 (DEAD IMPLANTS TAKEN AS A SUBSET OF IMPLANTS)

WEEK	CONTROL					71-71 12 MG/KG					71-71 120 MG/KG					71-71 1200 MG/KG					TEM			
	N	PRG	MEAN	STD DEV	DF	N	PRG	MEAN	STD DEV	DF	T	N	PRG	MEAN	STD DEV	DF	T	N	PRG	MEAN	STD DEV	DF	T	
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SINGLE TREATMENT																								
1	15	.44	.24	20	.44	.19	33	.022	16	.69	.55	29	1.620	19	.43	.30	32	.088	17	1.05	.55	30	3.970	
2	20	.45	.28	19	.54	.32	37	.907	16	.52	.30	34	.784	20	.52	.31	38	.785	20	1.97	.98	38	6.674	
3	20	.51	.38	20	.55	.31	38	.306	18	.61	.59	36	.642	20	.43	.21	38	.891	20	2.27	.72	38	9.643	
4	20	.46	.20	20	.61	.34	38	1.790	20	.52	.28	38	.860	20	.50	.36	38	.521	17	2.53	.36	35	22.037	
5	20	.63	.34	20	.58	.39	38	.477	20	.53	.29	38	1.009	19	.68	.39	37	.368	20	1.09	.54	38	3.212	
6	20	.57	.30	20	.48	.33	38	.906	20	.42	.22	38	1.761	20	.53	.53	38	.306	20	.40	.22	38	2.067	
7	20	.53	.47	20	.48	.27	38	.383	20	.51	.28	38	.196	20	.49	.34	38	.276	20	.51	.27	38	.203	
8	20	.59	.37	20	.54	.35	38	.433	20	.55	.37	38	.314	20	.49	.24	38	1.005	20	.57	.36	38	.160	
MULTIPLE TREATMENT																								
1	20	.86	.58	18	.59	.36	36	1.747	16	.57	.31	34	1.831	17	.49	.29	35	2.391						
2	20	.63	.32	17	.60	.41	35	.227	19	.49	.26	37	1.470	20	.54	.35	38	.818						
3	20	.56	.36	17	.73	.40	35	1.350	20	.72	.49	38	1.166	20	.41	.19	38	1.622						
4	20	.72	.41	18	.77	.65	36	.278	20	.55	.28	38	1.577	19	.49	.28	37	2.019						
5	18	.58	.39	18	.72	.52	34	.899	20	.67	.60	36	.537	20	.58	.33	36	.001						
6	20	.43	.24	17	.41	.28	35	.306	19	.49	.25	37	.731	18	.45	.20	36	.202						
7	20	.67	.58	16	.55	.43	34	.703	20	.50	.23	38	1.192	20	.37	.24	38	2.096						

CONTROL GROUP ANOVA FOR THE NUMBER OF PREGNANT FEMALES

WEEK	BETWEEN MALES			WITHIN MALES			TOTAL			F
	SUMSW	DF	MEANSQ	SUMSQ	DF	MEANSQ	SUMSW	DF		
SINGLE TREATMENT										
1	1.250	9	.139	2.500	10	.250	3.750	19		.556
2	0.000	9	0.000	0.000	10	0.000	0.000	19		I
3	0.000	9	0.000	0.000	10	0.000	0.000	19		I
4	0.000	9	0.000	0.000	10	0.000	0.000	19		I
5	0.000	9	0.000	0.000	10	0.000	0.000	19		I
6	0.000	9	0.000	0.000	10	0.000	0.000	19		I
7	0.000	9	0.000	0.000	10	0.000	0.000	19		I
8	0.000	9	0.000	0.000	10	0.000	0.000	19		I
MULTIPLE TREATMENT										
1	0.000	9	0.000	0.000	10	0.000	0.000	19		I
2	0.000	9	0.000	0.000	10	0.000	0.000	19		I
3	0.000	9	0.000	0.000	10	0.000	0.000	19		I
4	0.000	9	0.000	0.000	10	0.000	0.000	19		I
5	1.800	9	.200	0.000	10	0.000	1.800	19		K
6	0.000	9	0.000	0.000	10	0.000	0.000	19		I
7	0.000	9	0.000	0.000	10	0.000	0.000	19		I

CONTROL GROUP ANOVA FOR THE NUMBER OF IMPLANTATIONS PER PREGNANT FEMALE

WEEK	BETWEEN MALES			WITHIN MALES			TOTAL			F
	SUMSQ	DF	MEANSQ	SUMSQ	DF	MEANSQ	SUMSQ	DF		
SINGLE TREATMENT										
1	123.800	9	13.756	51.000	5	10.200	174.800	14		1.349
2	42.200	9	4.689	40.000	10	4.000	82.200	19		1.172
3	26.250	9	2.917	29.500	10	2.950	55.750	19		.989
4	59.050	9	6.561	63.500	10	6.350	122.550	19		1.033
5	75.200	9	8.356	147.000	10	14.700	222.200	19		.568
6	39.000	9	4.333	32.000	10	3.200	71.000	19		1.354
7	175.200	9	19.467	207.000	10	20.700	382.200	19		.940
8	19.450	9	2.161	17.500	10	1.750	36.950	19		1.235
MULTIPLE TREATMENT										
1	71.050	9	7.894	65.500	10	6.550	136.550	19		1.205
2	24.450	9	2.717	18.500	10	1.850	42.950	19		1.468
3	63.250	9	7.028	94.500	10	9.450	157.750	19		.744
4	251.800	9	27.978	105.000	10	10.500	356.800	19		2.665
5	132.778	8	16.597	203.000	9	22.556	335.778	17		.736
6	25.200	9	2.800	40.000	10	4.000	65.200	19		.700
7	57.050	9	6.339	119.500	10	11.950	176.550	19		.530

CONTROL GROUP ANOVA FOR THE PHE-1 PLANTATION LOSS PER PREGNANT FEMALE

WEEK	BETWEEN MALES			WITHIN MALES			TOTAL			F
	SUMSQ	DF	MEANSQ	SUMSQ	DF	MEANSQ	SUMSQ	DF		
SINGLE TREATMENT										
1	71.550	9	7.950	65.000	5	13.000	136.550	14		.612
2	24.450	9	2.717	28.500	10	2.850	52.950	19		.453
3	7.450	9	.828	5.500	10	.550	12.950	19		1.505
4	12.050	9	1.339	18.500	10	1.850	30.550	19		.724
5	42.800	9	4.756	72.000	10	7.200	114.800	19		.660
6	14.000	9	1.556	14.000	10	1.400	28.000	19		1.111
7	86.200	9	9.578	95.000	10	9.500	181.200	19		1.008
8	1.450	9	.161	5.500	10	.550	6.950	19		.293
MULTIPLE TREATMENT										
1	43.450	9	4.828	75.500	10	7.550	118.950	19		.639
2	24.200	9	2.689	21.000	10	2.100	45.200	19		1.280
3	25.450	9	2.828	45.500	10	4.550	70.950	19		.621
4	89.800	9	9.978	115.000	10	11.500	204.800	19		.868
5	123.444	8	15.431	101.000	9	11.222	224.444	17		1.375
6	38.800	9	4.311	37.000	10	3.700	75.800	19		1.165
7	30.050	9	3.339	32.500	10	3.250	62.550	19		1.027

CONTROL GROUP ANOVA FOR THE NUMBER OF DEAD IMPLANTS PER PREGNANT FEMALE

WEEK	BETWEEN MALES			WITHIN MALES			TOTAL			F
	SUMSU	DF	MEANSU	SUMSQ	DF	MEANSQ	SUMSU	DF		
SINGLE TREATMENT										
1	9.437	9	1.049	.500	5	.100	9.937	14		10.486
2	7.800	9	.867	3.000	10	.300	10.800	19		2.889
3	18.200	9	2.022	23.000	10	2.300	41.200	19		.879
4	3.450	9	.383	3.500	10	.350	6.950	19		1.095
5	20.200	9	2.244	19.000	10	1.900	39.200	19		1.181
6	6.250	9	.694	7.500	10	.750	13.750	19		.926
7	2.050	9	.228	2.500	10	.250	4.550	19		.911
8	25.050	9	2.783	29.500	10	2.950	54.550	19		.944
MULTIPLE TREATMENT										
1	38.250	9	4.250	21.500	10	2.150	59.750	19		1.977
2	17.800	9	1.978	12.000	10	1.200	29.800	19		1.648
3	27.800	9	2.533	15.000	10	1.500	37.800	19		1.689
4	15.450	9	1.717	43.500	10	4.350	58.950	19		.395
5	12.000	8	1.500	24.500	9	2.722	36.500	17		.551
6	5.000	9	.556	10.000	10	1.000	15.000	19		.556
7	10.450	9	1.161	24.500	10	2.450	34.950	19		.474

CONTROL GROUP ANOVA FOR THE RATIO OF DEAD IMPLANTS TO TOTAL IMPLANTS PER PREGNANT FEMALE

WEEK	BETWEEN MALES			WITHIN MALES			TOTAL			F
	SUMSQ	DF	MEANSQ	SUMSQ	DF	MEANSQ	SUMSQ	DF		
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SINGLE TREATMENT										
1	.045	9	.005	.003	5	.001	.048	14		8.413
2	.093	9	.010	.031	10	.003	.124	19		3.297
3	.147	9	.016	.185	10	.019	.332	19		.683
4	.020	9	.002	.022	10	.002	.042	19		1.001
5	.129	9	.014	.100	10	.010	.229	19		1.434
6	.069	9	.008	.091	10	.009	.159	19		.839
7	.416	9	.046	.514	10	.051	.929	19		.899
8	.146	9	.016	.168	10	.017	.314	19		.964
MULTIPLE TREATMENT										
1	.627	9	.070	.526	10	.053	1.153	19		1.323
2	.122	9	.014	.088	10	.009	.211	19		1.538
3	.163	9	.018	.087	10	.009	.250	19		2.093
4	.147	9	.016	.220	10	.022	.367	19		.742
5	.125	8	.016	.240	9	.027	.365	17		.584
6	.028	9	.003	.055	10	.006	.083	19		.564
7	.504	9	.056	.564	10	.056	1.069	19		.993

T-TEST OF THE NUMBER OF CORPORA LUTEA IN PREGNANT FEMALES